Understanding Rational Therapeutics

Therapeutics is something more than prescribing drugs

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Preface

This book has been written with a concern for the problem of irrational trends and practices in therapeutics. It focuses on the applied aspects of therapeutics, an understanding of which can facilitate physicians to approach and intervene in a clinical situation in a rational, scientific and logical manner.

The book has been divided into three sections. The first section provides fundamentals of rational therapeutics. In it are discussed how a patient should be approached and what factors should be taken care of to make a therapeutic decision as rational as possible. Effective communication is an important factor for an effective therapeutic relationship; the section therefore starts with a discussion on the process of communication. Next few chapters discuss what factors are to be taken care of when planning a therapeutic intervention, how to remain up-to-date- about therapeutics, and how to write a prescription to make it maximally useful. Post-prescription-writing factors like observing the patient for desired and undesired effects of the treatment and monitoring him for compliance are overlooked by physicians on many instances and their significance in rational therapeutics is discussed in the last chapter of this section.

Section two of the book aims at providing physicians an insight into the factors that influence their therapeutic judgement and decision-making. Because the medical school training provides the knowledge and skills on the basis of which physicians practice therapeutics, the first chapter of the section emphasizes the significance of medical school training. In the absence of any formal ongoing training of physicians, and in view of the difficult access to unbiased and objective information on therapeutics, the pharmaceutical manufacturers bear a strong influence on physicians. The effects of this influence are discounted in the second chapter of the section. The last chapter of this section describes various patient and doctor factors that influence physicians' clinical approach. Governmental and regulatory factors also have a significant influence on the way therapeutics is practised in a country, but because of the complexity of these factors and my limited awareness about them, they have not been discussed in the current edition of this book.

Last section of the book highlights the commonly observed irrational trends in the use of some common drugs. In addition to recognizing the irrational tends, guidelines on their rational use have also been provided. Drugs categories that are discussed include antibiotics, psychotropics, nonsteroidal antinflammatory drugs, antiepileptics, and vitamins. Drugs used for the relief of gastrointestinal symptoms are also among the commonly misused group of drugs but, due to reasons, they could not be included in this edition of the book. Last chapter of this section focuses on the group of drugs that have been considered as "undesired" by experts and generally their use is not recommended.

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Section 1

Essentials of Rational Therapeutics

"It is clear that drug therapy involves a great deal more than matching the name of the drug to the name of a disease; it requires knowledge, judgment, skill and wisdom, but above all a sense of responsibility."

"Laurence DR, Bennett PN. Clinical pharmacology. Edinburgh; Churchill Livingstone. (7th ed.) 1992. p2."

Chapter 1

Effective Communication - The Backbone Of Rational Prescribing

Therapeutic relationship between a doctor and a patient is a form of professional helping relationship in which patient reports to a doctor, the helper, to get help for his suffering or ailment. The relationship is established as an implied contract when a patient consults a doctor for help and the doctor shows his willingness to offer it. In this relationship patient relies on his doctor for skilled diagnosis, effective therapy, and human recognition of his suffering[1]. The ethical (and legal) responsibility of the doctor in this relationship is to offer all the possible professional help and if things are beyond his professional competency and/or resources then guide or refer the patient accordingly.

The doctor-patient relationship is primarily based on exchange of information; the patient informs the doctor about his ailment, who systematically processes it and in return informs the patient about the nature and course of the illness and details of the treatment. Exchange of such information is based on the process of communication. Understandably effective communication between patients and doctors is important to practice medicine effectively[2] and is crucial for delivery of quality health care[3,4].

Historically, the professional ideal of the doctor-patient relationship held that the doctor directed care and made decisions about treatment; the patient's principal role was to comply with "doctor's orders". This approach, referred to as 'paternalistic approach', has generally been replaced by the concept of shared decision making in the developed countries[5]. In this new approach, both doctor and patient make active and essential contribution in making a therapeutic decision. With growing awareness and options of treatment forms and facilities available, patients in the developing countries also tend to look into the help offered to them critically, desire to learn about their illness and the treatment they are offered, and participate in decision making. Therefore the concept of shared decision making is gradually replacing the paternalistic model in these countries as well. Because this new approach involves frequent discussion with the patient to ensure that they are well informed about the nature of their illness and the treatment alternatives, the significance of doctors' adeptness in communication further increases.

Effective communication between physicians and patients is crucial for the delivery of quality health care[6]. No treatment protocol is maximally effective if a good doctor-patient relationship has not been established[7], and effective communication is essential to develop a good relationship. Poor or ineffective communication in a therapeutic relationship can mislead the doctor in his therapeutic efforts and result in wrong diagnosis and wrong treatment. It also is an important reason of patient dissatisfaction and a source of avoidable distress and suffering. A study assessed the degree of stress associated with hospitalization by having a large number of surgical and medical patients rate aspects of their hospitalization in terms of perceived stressfulness[8]. Many of events or circumstances rated as most stressful related not to physical comfort or environmental aspects of hospitalization but rather to communication or absence of good communication between patients and hospital staff. The following were perceived as highly stressful for many patients:

- not being told their diagnosis,
- having their questions ignored,
- not knowing the reasons for or the results of the treatment, and
- perceiving the staff as using medical jargon and being in a constant rush.

Bakal (1979), in reviewing these events, concluded that "[such] problems are easy to solve by improving communication between the health professional and the patient[8]".

Of further concern is that although physicians often believe they do an adequate job of communicating with their patients, in fact what physicians think they are communicating and what patients actually understand does not always coincide[9]. One of the recent considerations, therefore, is that more attention should be devoted to the development of attitudes and skills at the expense of the current preoccupation with technical knowledge[2].

Developing Effective Communication Skills*

In the past, the view that good communicators or interviewers were "born and not made" was a common one. However a substantial body of evidence now supports the view that good communication skills can be learned[10]. People who appear to be "born interviewers" have, in fact, observed, learned, and practised successful communication skills in other aspects of their lives and have adapted, integrated , and used those skills in patient care.

Human communication is a deceptively complex process. The ability to communicate effectively can be learnt by recognizing the elements, levels, and pattern of communication and acquiring thequalities that can help communicate effectively.

*The format of the following discussion has been adapted from; Cormier LS, Cormier WH, and Weisser RJ, Jr. Interviewing and helping skills for health professionals. California: Wadsworth Inc, Belmont 1984.

Elements, Levels, And Patterns Of Communication

Elements of communication

There are five recognized elements of a communication exchange: sender, receiver, message, feedback, and context. As is obvious from the words, sender is the person who provides an information or message to a person, the receiver, who receives it. After receiving a message and interpreting it according to his knowledge and understanding, the receiver makes a response to it which is referred to as the feedback. The feedback guides people in adjusting the messages they send to one another and is helpful in clarifying communication. The time, place, physical setting or situation in which communication takes place is the context of communication. During any interaction, communication of message and feedback both occur at two levels, verbal and nonverbal levels (discussed below). In a face to face communication, the participants keep on changing positions from a sender to a receiver; in a therapeutic interaction, patient is the sender when he is informing the doctor about his illness, and doctor acts as the sender when he is informing a patient about the details of the illness and its treatment.

Although this introduction may make a communication exchange seem relatively cut-and-dried, communication rarely occurs so easily. Perhaps the greatest problem with communication in health care is the assumption that communication is an easy thing to do well. This assumption is only half true. It is easy to communicate but it is difficult to communicate well[11]. Various factor complicate the process of communication; the important ones are:

1. Context is the physical setting or the time and place in which the communication takes place. The same message communicated in different contexts is likely to convey different meanings and have different significance. It is, therefore, important to take into consideration the context in which communication exchange is taking place to effectively interpret the meaning of the communication.

2. Not only does the meaning of a message depend on the context of the message, it is also subject to the way in which the message is delivered and interpreted. Misinterpretation of communication between people is a common problem and is known as miscommunication[12]. An important reason for miscommunication is that there is often a discrepancy between the message a person wants to send, the manner in which he or she sends it, and the way receiver interprets it. For example, if a doctor tells a patient that " he would like to see him after five days", without exactly explaining why he would like to do so, the patient can interpret this in many ways, including some of the following:

   - The doctor is not clear about the diagnosis, has prescribed the medicine as a trial, and would like to see the effects after a few days.
   - He has some serious problem that needs to be reviewed after few days.

- The treatment is to be taken for five days and then discontinued if the advised follow-up cannot be complied to.

3. Another important reason for miscommunication is that the sender and the receiver may consider different parts of the message as the most important. Generally, the most significant aspect of a message is that part of a message that is assimilated by the receiver. Unfortunately, in many cases this may not be the part of the message that is critical to the sender. For instance, a patient may describe a number of symptoms to an interviewer and reveal that, as a result of the symptoms she has become apprehensive, because her mother had similar symptoms before she was diagnosed to have gastric carcinoma. The interviewer may concentrate on the description of the symptomatology and neglect the patients expression of fear, which for the patient may have been the more critical part of the message.

Two levels of communication

Senders and receivers communicate simultaneously on two levels during speech and during silence - the verbal and nonverbal levels, and both these levels of communication need to be recognized to communicate effectively.

Verbal level of communication refers to the words spoken or the objective report given by the sender during a communication, and comprises the content of communication. Verbal communication is denotative in function, in which words are used to denote, designate, or make known a particular idea or piece of information. Written language is also a form of verbal communication.

Nonverbal level of communication refers to the body language or subjective expression of sender during a communication. It includes all the unspoken communication that occurs between two persons and includes such elements as voice, inflection, tone, volume, gestures, posture, demeanour, mood, appearance, physical distance, and facial expressions (Table 1). It is also referred to as the process of communication. Nonverbal communication is connotative in function; i.e., body language is used to connote, imply, or suggest the presence of an idea or a piece of information.

Significance of nonverbal communication

Nonverbal messages are usually more spontaneous than verbal messages. They provide clues to the underlying feelings and emotions, and are usually more reliable than verbal clues[13]. They can also provide important behavioral signs that may reveal various difficulties or problems of the patient not expressed by him verbally. The importance of "reading" patients nonverbal messages, thus, cannot be overemphasized.

Table 1. Nonverbal Cues in Communication.

Feature	Examples
Body position	Tense, relaxed, leaning toward or away
Eyes	Teary, open, closed, excessive blinking
Eye contact	Steady, avoiding, shifty
Body movement	Knee jerks, taps, hand and leg gestures, fidgeting head nodding, dependence on arms and hands for expression
Body posture	Stooped shoulders, rigid, relaxed, legs crossed
Mouth	Smiling, lip biting, licking lips, tight, loose
Facial expression	Animated, bland, distracting, frowning, puckers grimaces
Skin	Blushing, pale, perspiration
General appearance	Clean, neat, sloppy, well groomed
Voice	Fast, slow, jerky, high pitched, whispers

Reproduced from: Okun BF. Effective helping: Interviewing and counselling techniques. California: Wadsworth Inc., Belmont 1982. p56.

Because it is easier to be attentive to objective reports than to subjective elements of communication, the verbal report of patients is the level that many health professionals notice the most. It needs to be realized that verbal self report can be limited by anxiety, lack of knowledge, fear, embarrassment, hostility and so forth. By ignoring a patient's nonverbal communication, therefore, the doctor may be missing a very important and accurate source of information.

Reading patient's nonverbal messages requires the interviewer to observe the patient carefully in all phases of the interview. Taking notes and looking at patient's chart while communicating with patient is a common barrier to "reading" body language. Even more frequent, however, is the simple failure to observe the patient carefully, and to notice the communication that is not being provided in words.

Both verbal and nonverbal communication are important for understanding patients' messages. These two levels of communication are interdependent. If both these channels of communication are given due importance and considered together, the true meaning of a communication is rarely missed.

Two patterns of communication:

There are two patterns of communication, congruent and incongruent. In a congruent communication pattern everything the person says and does is consistent, that is, the verbal and nonverbal messages sent to the receiver "match" each other. It is not uncommon, however, for patients to exhibit incongruent communication, in

which the verbal message and the body language contradict each other. Lack of congruence between the verbal and nonverbal messages may indicate that something is being omitted, whether deliberately or unconsciously, and such messages demand special attention and exploration. It is extremely important for the doctor to be congruent in his expression as well. If incongruent, the patient will feel uncomfortable in the communication exchange and effective therapeutic relation will be difficult to develop.

Doctor as a sender in the communication process

In the discussion so far patient has been considered as a sender but in a therapeutic relationship doctor also acts as a sender. Doctor is the sender when he is exploring patient's history, is explaining to him about the nature of the illness and is giving him the details of the treatment. It is important for the doctor, therefore, to be congruent in his communication, to give nonverbal expressions that convey concern, understanding and empathy, and to respond verbally in a manner that facilitates communication and makes it gaol-directed (Box 1).

Guidelines to facilitate effective communication

Means by which effective communication can be facilitated are:

1. Try to communicate in the same language and vocabulary the patient is using.
2. Speak slow enough so that the patient is able to follow you.
3. Be attentive to the patient, show your concern both verbally and nonverbally, and avoid all the activities that can impede the process of effective communication.
4. Use concise rather than rambling statements.
5. Pursue the topic introduced by the patient unless it is too out of context.
6. Send "I" statements to "own" your feelings and understanding, and allow the patient to reject, accept, or modify your messages.
7. Encourage the patient to express his/her feelings and point of view.
8. Time your responses to facilitate, not block, communication.

Characteristics Of Doctor That Help Develop Effective Therapeutic Relationship

People in different professions have to have certain profession-specific qualities to be effective and successful, and the same is true for doctors. A doctor is viewed by his patients to have certain qualities in addition to his professional competency. As Mechanic puts it: "Not only is the physician regarded as a man of knowledge and science capable of ferreting out the meaning of puzzling symptoms, but also he

frequently is pictured as a kindly, thoughtful, warm person, deeply interested in and committed to the welfare of the individual[14]".

Box 1. Verbal responses by doctor that can make communication with patients effective

The ten major verbal responses that can make communication with a patient effective are:

1. **Minimal verbal response**. They are the verbal counterpart of occasional head nodding and include verbal responses like "hunm", "yes", "I see", "right". They indicate that the doctor is attentive to and is understanding what the patient is saying.
2. **Paraphrasing**. A paraphrase is a verbal statement that is repetition of patient's statement in similar but different words. It helps to convey to the patient that his statements are being followed.
3. **Probing**. Probing is an open-ended attempt to obtain more information from the patient and is most effective when done using statements like, "tell me more", let's talk about that", "I'm wondering about" rather than "how", "what", "when", "where", and "who" questions.
4. **Reflecting**. Reflecting refers to communicating to the patient our understanding of his or her concerns and perspectives. We can reflect stated or implied feelings, what we have observed as nonverbal expression of the patient, what we feel has been omitted or emphasized, and any specific content.
5. **Clarifying**. Clarifying is an attempt to focus on or to understand the basic nature of a patient's statement that needs clarification or elaboration.
6. **Checking out**. Checking out means to check out or confirm any statement of the patient which the doctor has not followed, or regarding which he is confused.
7. **Interpreting**. Interpreting occurs when the doctor adds something to the patient's statement to help the patient to gain an understanding of his/her underlying feelings, and their relation to the verbal message. For a correct interpretation the doctor is likely to get a response like "yes, that's it", from the patient, for a wrong interpretation the response will be like "no, not that but....
8. **Confronting**. Confronting involves providing the patient with an honest feedback about what is really going on or to focus on statements and behaviour that reflects discrepancy.
9. **Informing**. Informing means providing factual and objective information to the patient. It differs from advising which is subjective and aims at telling the patient what to do and what not to do.
10. **Summarizing**. Summarizing is a form of clarification that is done after each major section of the interview is over. During summarization the details provided by the patient are summarized and communicated back to the patient. It helps to clarify discrepancies between the way the patient intended to convey the message and the way the doctor followed it.

Adapted from: Okun BF. Effective helping: Interviewing and counselling techniques (2nd ed.). Wadsworth, Inc., Belmont, California 94002. 1982. p61-63.

Because in a therapeutic relationship a doctor is the helper, he primarily needs to possess the characteristics of a good helper. These characteristics are briefly discussed below under two headings:

1. Characteristics that facilitate the therapeutic relationship
2. Characteristics that enhance the therapeutic relationship.

Characteristics that facilitate the therapeutic relationship

Three characteristics are recognized to facilitate the therapeutic relationship. These are empathy, respect, and genuineness.

Empathy

Empathy is the capacity to respond to another's feelings and experiences as if they were your own. It means, as the phrase goes, "putting yourself in the other person's shoes". Responding empathically to a person is an "attempt to think with, rather than for, or about" the person.

Empathy is a critical variable in influencing the quality and effectiveness of a helping relationship. It is both a relationship-establishing skill and a data-gathering or problem-clarification skill. It is helpful in developing rapport with and elicit information from the patient.

Empathy is both an attitude and a skill. A doctor's desire to understand and to be with the patient reflects his empathic attitude. This attitude, however, has to be translated into actions or skills so that it gets communicated to the patient that the doctor is empathic.

Respect or positive regard

Respect or positive regard means the ability to value the patient as a person with worth and dignity. Doctors should be able to give positive regard to patients regardless of who they are and what they do. Respect is an attitude, an inner quality that reflects a way of considering people or patients and like empathy, it needs to be translated into actions to affect the relationship.

Raush and Bordin (1957) and Egan (1982) have identified four components of respect[15]:

- having a sense of commitment to the patient;
- making an effort to understand the patient;
- suspending critical judgment; and

- expressing a reasonable amount of warmth.

Commitment

Commitment to the patient implies some degree of willingness and interest in working with the patient. Like empathy and respect, the attitude of commitment must be felt by the patient. Scheduling spending a specific amount of time to see the patient, ensuring relative privacy and confidentiality during the therapeutic encounter, being attentive to him while he is talking, and applying professional skills to help the patient, all help in communicating commitment to the patient.

Bernstein and Bernstein (1980) have observed the serious and negative consequences that result when such commitment on the part of the health professional is missing. They state:

> *"From the point of view of the patient, then the most serious barriers to a good relationship (and consequently better diagnosis and treatment) are the professionals lack of time, his seemingly lack of concern, and his failure to tell the patient what he needs to know and can understand about his illness. Repeatedly in studies and surveys when patients are asked about their opinion about medical care they respond critically and often bitterly about the doctor's or nurse's hurry when taking care of them. This hurry is apt to be interpreted - and resented - not as lack of time, but as a lack of humane interest in the sick individual*[15]."

A properly expressed commitment conveys to the patient a feeling of connectedness with thephysician. This reduces his feeling of isolation and eases his despair that are consequence of illness. Such a feeling of connectedness is the very heart of healing. Wholly independent of whatever biotechnical treatment is offered, this deep transpersonal connectedness between the patient and doctor is comforting and therapeutic[16].

Understanding

Patients will feel satisfied to the degree that they feel the health care provider is attempting to understand them. Physicians who attend to their patients in an indifferent manner are usually unable to develop an effective therapeutic relationship. An effort to demonstrate understanding can be conveyed to a patient by being empathic, by asking questions designed to elicit information important to him, and by indicating with actions and comments the interest in understanding the patient.

Nonjudgmental attitude

A nonjudgemental attitude refers to the interviewer's ability to suspend judgement of the patient's actions or motives and to avoid condemning or condoning his/her

personality or behaviour. It implies the ability to be accepting rather than being critical of the patients. It does not necessary mean that the doctor should support or agree with all the patient does or says. Rather, the doctor should be able to create an atmosphere in which the patient feels comfortable and is able to respond to doctor's opinions and options when they are introduced.

A nonjudgmental attitude is conveyed by the doctor when he warmly accepts patient's expressions and opinions without imposing conditions. In contrast, whenever a doctor expresses dislike or disapproval regarding the motives, actions, personality, or behaviour of a patient, he is conveying a judgmental attitude.

Warmth

Warmth is a key component of any effective interaction because most people respond to warmth with warmth and conversely, to hostility with hostility. According to Goldstein (1980), without the expression of warmth, specific procedures "may be technically correct but therapeutically impotent[17]".

Warmth can be expressed to the patients through specific verbal statements and nonverbal behaviours. Verbally, comments like, "you expressed your problem well", "you have a good understanding of your illness", "you have really done a good job by taking your medicine regularly", show warmth and enhance the therapeutic relationship. Nonverbal, warmth is communicated through tone of voice, facial expressions, gestures, and posture (Table 2).

Warmth is an indicator of patient concern. It does not mean praising the patient or being all to nice. Sometimes it may be expressed by directiveness, assertiveness, autonomy-enhancing distancing, and even anger. The presence of warmth also allows the doctor to confront the patient when necessary and appropriate.

Table 2. Nonverbal Cues of Warmth and Coldness.

Nonverbal Cue	Warmth	Coldness
Tone of voice	Soft, soothing	Callous, reserved, hard
Facial expression	Smiling, interested	Poker faced, frowning, indifferent
Posture	Relaxed, leaning forward	Tense, leaning away
Eye contact	Maintaining eye contact	Avoiding eye contact
Gestures	Open, welcoming	Closed, as if guarding oneself
Physical proximity	Close	Distant

Adapted from: Cormier LS, Cormier WH, and Weisser RJ, Jr. Interviewing and helping skills for health professionals. California: Wadsworth Inc., Belmont 1984, p30.

Genuineness

Genuineness refers to a person's ability to be sincere without presenting a facade. Genuine people are at home with themselves and therefore can comfortably be themselves in all their interactions. Because people generally relate better to someone who is genuine or "real", genuineness is helpful in the development of rapport and trust in the therapeutic relationship. Genuineness can be communicated to the patient in different ways.

Congruence

Congruence means that the doctor's words, feelings, and actions are consistent. Congruence also implies that the doctor is also aware of any discrepancy that exists between his feelings, words, and actions and is careful not to let such discrepancies interfere with the therapeutic relationship.

Role behaviour of doctor

Doctors who do not overemphasize their role are more likely to be perceived as genuine than those who constantly remind the patient of their role, position, authority, and status.

Spontaneity

The third aspect of genuineness is spontaneity. Spontaneity is the capacity to say or express oneself naturally, freely, and easily without acting in a contrived manner. It also implies the use of tact without conversational hesitancy. It, however, does not mean the doctor must verbalize every passing thought or feeling, nor does it previlidge the doctors to say whatever is on their minds. Effective doctors are spontaneous and assertive without being blunt and aggressive.

Genuineness is also communicated by the doctor's use of appropriate or supporting nonverbal behaviours. Nonverbal behaviours that convey genuineness include eye contact, smiling, and leaning towards the patient while communicating. These three nonverbal behaviours, however, should be used discretely; persistent eye contact (gazing) may be interpreted as staring, and continual smiling or leaning may be viewed as phoney and artificial, rather than as genuine and sincere.

Characteristics that enhance therapeutic relationship

In addition to characteristics that facilitate therapeutic relationship, there are characteristics that enhance the relationship by providing a doctor a base of influence. Doctor can use this base of influence to develop an effective therapeutic relationship. Three characteristics recognized to enhance a therapeutic relationship

are: competence (expertness), trustworthiness (credibility), and attractiveness (liking).

Competence

Competence or expertness is not merely the knowledge and skills a doctor possesses. It is also the patients' view about his competency. Competence (or perception of it) is extremely important in a therapeutic relationship. First, it enhances the patient's faith and belief in the doctor, and therefore, endows the doctor with an additional degree of authority. Second, competence is related to patient compliance. Patients are more favourably disposed to accept and act on the recommendations of someone whom they perceive as competent.

Three variables have been identified to contribute to a person's (patient's) perception of interviewer's (doctor's) competence[18]. These are role, reputation, and behaviour.

Role

Role refers to the doctor's title, position, and credentials. Role can be established very quickly, simply by the way doctors introduce themselves and by their dress, demeanour, office decor, and so on. Doctors who dress and act in concert with their role are apt to be perceived as more competent than those who do not. A doctor who dresses carelessly, slovenly, or inappropriately with reference to the social set-up he is practising, or who acts timid or uncomfortable is likely not to convey much role expertise to the patient.

Patients may also look at nameplates, diplomas, and certificates to establish the role expertness of a doctor. Therefore, it may be prudent to display the certificates and diplomas in the clinic. Such "external trappings" may serve the dual purpose of establishing role capability and enhancing the decor of an office or clinic.

Reputation

Reputation refers to the view people have about an individual's personality and competency in general. In health care, many patients seek to establish the reputation of health professional before deciding to seek the services. They may do so by asking the opinion of other patients, of other health professionals, or even by noting whether the person in question is associated with a prestigious or well-known institute. Unfortunately, reputation is not always a reliable indicator of the health professionals actual competence. In some instances, a very skilled health care worker may receive a "bad press". In other cases, a less well skilled health professional may be held in a very high esteem by others.

Behaviour

The third and most important aspect of competence is a behavioral one - whether professionals measure up to the expectations of their roles and reputations by demonstrating the necessary skills and knowledge for helping patients. The behavioral aspect of competence, therefore, is established by what the doctor actually is able to accomplish with the patient. If things progress according to patient's expectations, the therapeutic relationship lasts. But if little or nothing is gained, the relationship is likely to get severed in spite of doctor's excellent role and reputation.

Trustworthiness

Trustworthiness or credibility is another characteristic that enhances a therapeutic relationship. It can be defined as "an expectancy held by an individual or group that the word, promise, verbal or written statement of another individual or group can be relied upon". Patients who view the doctor as trustworthy are likely to be cooperative. Trustworthiness or credibility is critical in a therapeutic relationship. Lack of trust or confidence in a doctor can endanger the entire treatment process. Sadly this simple requirement is often neglected, even by health care workers who expect their patients to commit their lives and welfare to them, albeit briefly. When health professionals establish a trusting relationship with their patients, "the patients recover quicker, experience less pain, and experience a greater variety of physiological, psychological and behavioral gains[19]".

Trustworthiness is communicated in several ways. Like competence, trust in a doctor may be enhanced simply because of a reputation for honesty and the social role. Patients are more likely to trust a doctor if they have heard descriptive statements about him confirming his honesty and scrupulousness. Different ways in which trustworthiness can be communicated to patients are:

1. Always provide accurate and reliable information to patients. There is no justification in providing false or inaccurate information even when the intentions are divine, as it can do more harm than good in the long run. If a patient inquires about something that you do not know or you are uncertain of, accept your ignorance or look into the books before conveying it to the patient.

2. Be dependable; the patient is depending on you for his health. The essence of dependability is that, do not promise what you cannot do, and be sure to deliver what you promise. However it should be noted that over-dependence of a patient is detrimental to the therapeutic relationship and should be discouraged.

3. Maintain confidentiality of the patient's communications. Nothing will destroy trust more quickly than a patient's discovery that confidential information has been shared with somebody else without prior permission from him.

4. Respond to the patient with some degree of dynamism; a patient's level of trust will be decreased if the doctor is passive, lethargic, or inactive.

5. Demonstrate concern and sincerity in your motives and intentions. Avoid behaviour that might indicate the presence of ulterior motives like selfishness, superficial curiosity, or some personal gain.

Interpersonal attractiveness

A patients perception of the doctor's attractiveness is based on perceived similarity to, compatibility with, and liking for the doctor. Interpersonal attractiveness is helpful in developing a compatible working relationship with patients. Doctors are likely to have greater influence on patients if patients like them and perceive some degree of similarity between themselves and the doctor. Physical characteristics and general appearance may influence the patients perception of the doctor and therefore it is important that the dress and manners of doctor should be socially appropriate and acceptable to the setting where he is practising. Role, reputation, and interpersonal behaviour are other factors that enhance a doctor's perceived attractiveness, and they should be taken proper care of. If patients perceive the doctor as attractive, the helping relationship will be strengthened and enhanced, and the patient will cooperate with the doctor to a greater extent. Presumably, doctors will have more influence with the patients who feel compatible with and like them.

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Chapter 2

Defining Patient's Problem - Something More Than Making A Diagnosis

Making a correct diagnosis is a crucial step in selecting the correct treatment. However, a treatment selected only on the basis of diagnosis is not always "appropriate" for all the patients suffering from the same condition. This is because individual patients differ from each other in biological, psychological, and social aspects, come from different professions, and vary in their financial resources. Therefore "defining the patient's problem" is something more than merely making a diagnosis. It is "understanding the patient's illness in his context" and essentially can be considered to have two components:

1. Making a diagnosis.
2. Understanding the patient

Making A Diagnosis

The process of making a diagnosis is a problem-solving activity. In this process, doctor gathers necessary information from the patient, substantiates it with the physical examination and appropriate investigations, and analyses it in the background of his knowledge.

Traditionally ,a lot of importance is given to the process of making a correct diagnosis during the training in clinical years and medical graduates are well aware of its significance. The training, however, has certain limitations in its social applicability (for details see chapter 7). The main reason for these limitations is that the setup where training is conferred significantly differs from the situation where most (almost all) fresh graduates have to work after completion of their internship. During the clinical and internship training, time is never deemed as a barrier to patient evaluation, the institutes are well equipped with investigation facilities, and there are many seniors to identify the deficiencies and guide accordingly. In contrast, most doctors after completion of internship have to work unsupervised in situations that are usually crowded with patients and have limited investigation facilities. The major consequence of this discrepancy is that fresh graduates have to mould their training according to their working situation. During this process of adaptation, influenced by various social and professional pressures, doctors are likely to learn some irrational

ways of patient evaluation and management. The following section provides some practical considerations regarding patient evaluation with emphasis on commonly observed trends that can lead to irrational prescribing.

Art of history taking

To establish a diagnosis and initiate an appropriate treatment doctor requires some information about the patient and his symptoms. The desired information is gathered by what is called "history taking". Every doctor is aware of what to inquire when taking history of a patient; the formal headings under which inquiry is made are[1]:

1. Age, address, marital status, occupation and social circumstances.
2. Presenting complaints.
3. History of present illness.
4. Previous history of illness.
5. Menstrual history.
6. Treatment history.
7. Family history.
8. Social and occupational history.

An important aspect of history taking is how the patient is approached and inquiry is made, which is referred to as "the art of history taking" (Box 1). A doctor skilful in the art of history taking can effortlessly convey empathy, respect, concern, warmth and understanding towards his patients and consequently can develop an effective rapport and therapeutic relationship from the outset. Such a rapport with a patient makes the process of gathering relevant and useful information easy, facilitates the process of making correct diagnosis, and influences compliance of the patient to the suggested therapeutic regimen favourably.

Patients have few cues to assess a doctor's scientific medical knowledge and skill. An important mode by which they assess a doctor's competence is by evaluating his concern, thoughtfulness and commitment towards them[2]. Because a doctor skilful in the art of history taking can effectively express such feelings towards his patients, an additional advantage of knowing the art, therefore, is to be valued by patients and earn the reputation of a "competent doctor".

When lack of time is a barrier

The out-patient departments of referral institutes and other big hospitals are usually crowded with patients. Doctors working in these hospitals often feel and plead that they do not have enough time to systematically interview their patients. The situation seems to be one of the facts eventuating from poor health structure of many of the developing countries, but it does not provide grounds to justify poor interviewing skills. A doctor skilled in the art of history-taking can develop a better therapeutic

Box 1. The art of history taking.

A. BEGINNING OF THE INTERVIEW

Putting the patient at ease

- Greet patient and initiate the interview in a reassuring way.
- Show respect for patient and attend to his needs of privacy and comfort.

B. MIDDLE OF THE INTERVIEW

Eliciting information

- Use language appropriate to patient's age and background.
- Use open-ended questions.
- Let the patient explain things in his own words without unnecessary interruptions.
- Intervene with appropriate responses when patient is unable to provide relevant information.
- Rephrase or repeat question if needed to enhance understanding.
- Clarify areas of confusion or inconsistencies.
- Inquire as to how well patient understands his illness.
- Keep aware of your verbal habits (continuous okays, uh-huhs, noddings) that may be misunderstood by the patient.

Maintaining control

- Remain aware of the pace of the interview.
- Make periodic summarizations.
- Make clear transition from one step of the interview to another.
- Interrupt unnecessary patient rambling to maintain focus.
- Use pauses to encourage patient response.

Maintaining rapport

- Maintain eye contact.
- Use nonverbal aspects (office seating arrangement, body posture, facial expressions) appropriately.
- Provide opportunities to patient to express feelings about current illness and other problems.
- Share the feelings when appropriate.
- Accept patient's values in nonjudgmental manner.
- Avoid language or behaviour that may arouse patient anxiety.
- Explain the need for requesting certain data to reduce patient anxiety.
- Deal with patient's expressed questions and concerns.
- Deal with patient's nonverbally communicated concerns.

C. END OF THE INTERVIEW

Bringing closure

- Inform patient about dosage of drugs, their likely side effects, next follow-up etc.
- Allow patient opportunity to ask any questions.
- Provide closing statements which facilitate a comfortable ending.

Reproduced from: Kreps GL, Thornton BC. Health communication. New York: Longman Inc. 1984. p115-116.

relationship and extract more information from the patient in a given time than a doctor who approaches patients in a clumsy manner.

If lack of time does not permit to go into the details of all the headings of history-taking listed above, effort still should be made to no something about every aspect of patient. History-taking is not only directed to determine what a patient is experiencing, but also to discovering what sort of person is experiencing these symptoms. By foregoing inquiry into personal, social, professional, and financial aspects of patient's life one is likely to miss some important facts that can contribute to approaching the correct diagnosis and rational prescribing and, therefore, inquiry into these areas should never be omitted.

Whatever time can be allocated to a patient it should be attentively spent with him and distracting activities like attending phone calls and visitors should be avoided during the interview. A casual or hurriedly encounter with the patient can result in an erroneous diagnosis and initiation of wrong treatment, and should always be avoided.

The troublesome patient and the difficult doctor

Some patients are difficult to communicate with even when they are conversed with in their languages. Such patients, not infrequently, irritate the doctor and the process of communication becomes further difficult. The irritated doctor considers such patients as "troublesome patients", and the annoyed patient comes to view the doctor as a "difficult doctor".

Shyness, fear, or sheer "stupidity" are important reasons that may obstruct the process of history-taking. Many doctors seem to regard the first two sympathetically, but blame the patient for "stupidity" (usually a result of illiteracy and erroneous health believes). In point of fact it is the most excusable[3]. In addition, communication may also be difficult with patients who have an erroneous preconceived idea of the significance of their complaints or present with a self-made "diagnosis". Doctor may be tempted to refute such patients and get annoyed with them, thus, further thickening the communication barrier.

These patients need to be approached in a reassuring manner and effort has to be made to understand their believes and point of view. If the doctor is able to control his initial annoyance and reassure such patients, usually the process of effective communication starts and the "troublesome patient" and "difficult doctor" cease to exist.

Help of investigations in reaching a diagnosis

Laboratory, radiological, and other investigations are quite helpful in establishing a diagnosis, but it should always be remembered that they cannot substitute a

thorough clinical evaluation. In spite of the proliferation of modern diagnostic tests, history-taking and physical examination remain essential skills[4]. It also has to be born in mind that most of the investigations have inherent limitations. They are not absolutely sensitive or specific. That is, they can give negative results for patients suffering from the illness and positive results for patients who are healthy with reference to that specific illness. Investigations help only in confirming or rejecting a diagnosis provisionally made on clinical evaluation and, therefore, should never be asked for to *make* a diagnosis. Significance of a comprehensive clinical assessment further increases in countries where assess to reliable laboratories is limited and patients generally cannot afford costly investigations

Sometimes the patient or his family members are very keen to have some investigations done, believing that it is the only sensitive way of diagnosing the patient's illness. Though proceeding with the interventions desired or expected by patients might result in increased patient satisfaction[5], it is prudent not to accede to such demands spontaneously. If the specific investigation demanded is not required then yielding to patient's demand is comparable to prescribing an unnecessary drug on patient's desire and is equally irrational. It results in wastage of patient's resources and more importantly reinforces his misconception that investigations are always essential in understanding a disease. Instead of giving up to such demands with a justification that it will help satisfy the patient, or ignoring them altogether, it is important to have a discussion with such patients regarding their demands. Understanding their point of view and giving valid arguments in understandable terms are usually convincing and reassuring for such patients.

Uncertainty over a diagnosis

It is not uncommon for doctors to be confronted with the problem of uncertainty over a diagnosis. The reasons are numerous; the doctor may have incomplete or imperfect mastery of available medical knowledge, information provided by the patient might be patchy, clinical presentation might be vague and confusing, a reliable investigation facility might not be in the financial or geographical approach of the patient, or their might not be enough time to wait for the results of the investigations.

The situation of uncertainty over diagnosis is specially common in general practice settings, where 50% of the illnesses seen may not admit of a precise diagnosis[6]. An important factor contributing to the situation in these settings is that many patients with emotional problems present with minor and vague physical symptoms to the doctor. According to some estimates, up to 50% of all visits to primary care physicians are motivated by or are consequence of psychological or emotional problem[7].

Handling the situation

In such situations of uncertainty, the nature of the doctors adaptive strategies will frequently be influenced by the pressure on him and the contingencies of his practice[8]. As it is consoling for a doctor to make a diagnosis which is amenable to therapy, there is very real risk that the doctor diagnoses conditions for which therapy is available[9], even when he is not certain about the diagnosis. He also will frequently choose to treat rather than to wait, to gratify patients' expectations who see prescriptions as a "gift" at the end of consultation[10]. All these factors can lead a doctor to an irrational approach towards the situation and he should, therefore, remain at guard whenever he is confronted with the problem of uncertainty over a diagnosis. (Some of the commonly employed strategies in the situation are discussed in chapter 3).

Understanding The Patient

Individuals differ from each other in their biological, psychosocial, professional, and financial aspects. These individual characteristics predispose different individuals to different diseases, determine their behaviour in an illness situation and compliance to advised therapeutic regimen and, thus, influence the ultimate outcome. An understanding of these aspects of a patient, therefore, is important in effective and rational practice of therapeutics and its significance has long been appreciated. When Osler suggested that the patient was more important than the disease, he was emphasizing the importance of understanding the life circumstances and personality of the patient[11]. And according to Hippocrates:

> *"These things one ought to consider most attentively.....the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, and given to indolence, or are fond of exercise and labour, and are not given to excess in eating and drinking".*
>
> Hippocrates, "On Airs, Waters and Places".

Such an understanding of a patient is only possible through an inquiry into the socioeconomic background, family history, and personal history of the patient, and by formation of an opinion about his personality traits and beliefs.

Socioeconomic background

Social class is a composite measure of income, education, and occupation. An inquiry into the socioeconomic background of a patient is helpful in gaining insight into his education, nature of job, financial resources, and the available social support.

Socioeconomic status of a person affects his health status and interaction with the health care facilities in a multitude of ways. Patients from upper socioeconomic group usually are educated, perform jobs of sedentary nature, are financially well of,

and have a rich social life (but not necessarily a strong social support). They are more vulnerable to obesity and obesity related diseases like hypertension, diabetes mellitus, and ischemic heart diseases. Because of better financial affordability (and awareness) than persons from lower socioeconomic background, persons from upper and middle socioeconomic class are more likely to follow a healthy life style[12] and report to a doctor in the initial phase of illness.

As opposed to patients from upper socioeconomic group, those from lower socioeconomic group are usually less educated, are labourers and manual workers, have financial constrains, and a variable social life and support. They have been recognized to suffer disproportionately from ill health[13] and in general, the lower one's social class, the more vulnerable one is to illness and death[14,15]. Scarcity of balanced diet, overcrowded dwellings, shortage of water for washing purposes, unsafe drinking water, and poor sanitation facilities predispose them to malnutrition, and communicable diseases (infections and infestations). The problems of lack of food and unhealthy living conditions are compounded by ignorance and erroneous health believes. The poor also have been recognized as slower to seek treatment than those from upper class[16]. They are likely to consult a doctor late in the course of illness; only when the symptoms have become severe or a reason for personal/occupational disability. Even when they decide to get expert help the poor, due to financial constrains, are likely to consult an unqualified practitioner who may offer his services at a rate lesser than that of a qualified one, and reach a qualified doctor only when the disease has progressed and given rise to complications. While treating a poor patient the doctors should always keep the non-medicinal interventions in mind; many of the poor's health problems can be prevented and some of them can even be cured by such interventions (Box 2). Cost effectiveness is also an extremely important consideration while treating the poor. It needs to be realized that the poor have to make sacrifices to buy drugs[17]. When drugs contained on a prescription are beyond their financial resources, the poor are likely either to omit some of the drugs on the prescription altogether or to use the prescribed drugs in a dose and/or for a duration lesser than that has been advised. In both cases they will not effectively benefit from the prescription.

Patients' level of education

Education and social class have repeatedly been shown to influence the way patients use doctors[18]. An educated person is less likely to have erroneous health believes and more likely to be health conscious, aware of elementary concepts of hygiene, and vigilant in seeking help when sick than an uneducated one. Similarly, educational level of patient is an important determinant in a therapeutic relationship. All patients have a desire for and need to be informed about the nature of their illness, details of treatment and the expected outcome. An educated patient is easy to communicate with than an uneducated patient and consequently is more likely to be informed about such details than an uneducated one. A conscious effort, therefore, may be required to provide the relevant information to the uneducated patient. An uneducated patient is more likely to have erroneous health beliefs than an educated one. It needs to be appreciated that if such beliefs are not inquired into and discussed

may jeopardize the therapeutic intervention and relationship. It is difficult for uneducated patients, specially when the accompaniment and other family members are also uneducated, to understand, remember and comply to complicated therapeutic regimens. It is, therefore, sensible to keep their therapeutic regimen as simple as possible, explain it lucidly, and get the instructions repeated by the patient to ensure that he has followed them.

Box 2. Drugs are not the solution always.

The story of one little Bangladesh girl, struggling for life in a Children's Nutrition Unit in Dacca, is representative of the predicament of many of the world's poor.

She came from a village in Comilla, a district about 30 miles from Dacca. Her mother was poor, a widow, with five other children to feed. The little girl had fallen ill. She got progressively worse, so to get money for medicines and a doctor her mother sold some cooking pots and few other possessions. She even sold a small piece of land so that they could travel to the city. The doctors at the first hospital they tried said she would have to pay for the child to be admitted. So they went to Dacca Medical College. The doctors there examined the little girl and sent them away with a prescription for half a dozen drugs, mostly antibiotic and multivitamin tonics.

Her mother bought some but could not afford all the drugs. The child was getting weaker so she turned to some relatives for help. But they had nothing to spare. Fortunately, when the mother was getting desperate, some neighbours told her about the Save the Children Fund Nutrition Unit where she would not have to pay. By the time the little girl was admitted, she weighed just over 5 kilos (about 11 pounds). At the age of 6, she was only a little heavier than a newborn baby. The doctors diagnosed severe protein-energy malnutrition and anaemia. The child's life was in immediate danger because the haemoglobin level in her blood had dropped so low that her heart was in danger of stopping. That was not all. She had other complications, including chest infection, a urinary tract infection and worms.

To stand any chance of surviving, the child needed intensive nutrition treatment. She would have to be fed milk through a nasal tube because she was nearly unconscious, and she also needed several blood transfusions.

But her mother had been sent away to buy expensive medicines. Even if she had found the money to pay for them, they could not have saved the little girl's life. The prescription would have meant money down the drain, because the underlying cause of the child's serious condition was lack of food. The tragic irony of this little girl's case is that to get her to city, to see doctors and to buy medicines, her mother had been forced to sell the best guarantee of her children's health. Without that piece of land, it was going to be even harder to stop the other children from getting more seriously undernourished

"Source: Melrose D. Bitter Pills: medicines and the third world poor. Oxford: oxfam. 1987. p91".

Patients' occupation

People from different occupations are predisposed to different illnesses because of the nature of their jobs and exposure to specific chemicals, toxins, or environment. For example, a foundry worker works in a noisy and hot environment, and is exposed to silicon dioxide, asbestos, polycyclic aromatic hydrocarbons, and carbon monoxide; a mechanic works in a noisy environment and carries a risk of getting injured while operating the machinery; a taxi driver is exposed to exhaust fumes and dust; a computer operator spends most of time sitting in a posture that can cause him musculoskeletal strains; and a office executive is working in a state of urgency and stress most of the times. It is important for doctor to have an understanding of the symptoms and illnesses that can result from specific occupations and evaluate patient's illness in view of his occupation. If symptoms or disease of a patient are found to be related to his occupation then the patient should be advised for interventions by which he can avoid the symptoms or progress of the disease. Treating occupation related symptoms only with drugs is an indication of the doctor's limited therapeutic vision and is likely not to be of much benefit to the patient on most instances. Patient's occupation should also be taken into consideration when suggesting medicines with an effort to prescribe drugs that do not interfere with his occupational performance or increase the chance of occupational risks and accidents. If such a treatment is unavoidable then it is necessary to warn the patient of the possible side effects or recommend few days off from duty if required. Similarly, it should also be taken care of that the advised treatment is viable with reference to patient's occupation. Occupation of a patient also determines how much days he will be needing off work during an illness or after any therapeutic procedure. For example, a labourer operated for hernia will be needing more days of rest than an office worker undergoing the same operation.

Family structure, support and background

Every doctor knows that an inquiry has to be made into the family history of patients but most of them limit it to just asking about the family medical history. Even that is mostly inquired only in cases where a communicable disease or an illness having some genetic contribution is suspected. It needs to be appreciated that an inquiry into family history should extend beyond family medical history; an inquiry into family structure, support and background needs also to be made and has a significance of its own. It provides information that is helpful in understanding the patient, his illness and illness behaviour, and defining the therapeutic interventions.

Family is the environment in which a person grows and acquires attitudes, beliefs, and values about life including those about health and illness. Attitudes toward body size, cleanliness, and preventive health measures are learned at an early age and reinforced within the family context. A family's life style strongly influence a person's pattern of eating, drinking, and use of tobacco and other drugs. By inquiring into the family set up and background, and education and occupation of family members doctor can form an opinion about an individual's views about health and illness.

Formation of such an opinion can help the doctor to be more effective as a therapist. For example, it is not uncommon to come across patients who value obesity as a sign of health and maintain it by excessive intake of fat and cream products. A therapist who wants such a patient to loose weight is likely not to succeed unless he has recognized and attempted to correct the patient's (and other family member's) erroneous conception.

Similarly, the way a person interprets his bodily symptoms and seeks professional help is also affected by his family and cultural background. A person may be worried about and seek professional advise for medically trivial symptoms that are considered significant in his family and culture. For example, some families are preoccupied with and view minor gastrointestinal symptoms as a root to various serious ailments, and it is not uncommon to see such patients receiving symptomatic treatment for these minor complaints. A rational therapeutic approach for such patients is the recognition of the erroneous assumptions and appropriate education and reassurance. On other occasions a patient may be indifferent towards symptoms/illness of medical concern due to the same reason and thus will require interventions accordingly.

Patients are also likely to interpret their symptoms with reference to symptoms and illness of somebody in the family. For example, a patient of migraine might be extremely worried about his headache because he has witnessed his elder brother, a case of brain tumour, die of the same symptoms; a patient might be over concerned about his blood pressure since his hypertensive father developed hemiplegia Such patients can only be handled effectively after their association of the symptoms has been recognized and the patients are discussed with and reassured accordingly.

There is strong evidence that patients in every social, economic, and educational class seek and use alternative care[19] (i.e., care from someone else than a qualified allopathic doctor). When and from whom help is sought during an illness is determined by the beliefs of the patient and his family members. It is not unusual for a doctor to attend to patients who have tried some local remedies, and had been to local healers, unqualified practitioners and/or homeopaths before seeing him. The situation demands discussion with the patient and his family members to establish their trust and faith in the treatment, without which the therapeutic relation remains volatile. The discussion is specially beneficial when someone influential in the family is not convinced for treatment from a doctor.

The significance of inquiring into family structure is well recognized for effective intervention when treating a patient suffering from a communicable diseases like tuberculosis, scabies, worm infestation, and hepatitis A. In such situations it is not enough to tell the patient that the disease is communicable, close physical contact should be avoided, and towels and cloths etc. should not be shared. In addition, effort should me made that all the family members likely to be harbouring the illness are screened by a doctor and treated simultaneously so that the disease can be eradicated from within the entire family.

A child or an elderly patient is dependent upon his family members to consult a doctor and in such situations doctors have to involve the accompaniment in the therapeutic relationship. However, even when an adult reports to a doctor for help, family members can be an important therapeutic ally of the doctor. It is a good practice to incorporate family member/s in the therapeutic relationship if possible. By this incorporation doctor can learn more about the patient's illness, his family structure and cultural background. Family members can also be of help in ensuring patient's compliance with treatment and they can provide therapeutically relevant information to the doctor, on the basis of which he can monitor the treatment.

Family (and social) support may act as a buffer against certain kinds of illness. There is a good deal of evidence that the presence of various social supports has a positive influence on psychological states and general measures of morbidity as well as compliance with treatment regimens. Conversely lack of support or presence of stresses may predispose a person to certain illnesses[20]. By an understanding of patient's family setup a doctor can assess the support and stresses and provide guidance to the patient and his family members accordingly.

Personal history

An inquiry into patient's personal history aims at gathering data about his birth, mile stones of development and health in childhood, schooling and education, occupation, use of drugs, sexual history, marital history, details of previous illnesses, and present circumstances. Its significance in understanding a patient cannot be overemphasized and most doctors get at least a glancing account of patient's personal particulars. It suffices here to say that the most a patient can be understood is by an inquiry into his personal history and no matter how brief a therapeutic encounter is one should never forego it.

Personality and beliefs

What symptoms a patient thinks are important, when and from whom he seeks expert help, and how he interacts in a therapeutic relationship is generally an expression of his personality and beliefs. If a doctor is able to form an opinion about these attributes of a patient, the therapeutic relationship becomes more predictable and manageable for him than if he has not formed an opinion. An inability to understand patient's personality and beliefs can give rise to needless frustration in the relationship and result in a failure to accomplish the desired therapeutic objective. Many doctors who are unable to attract or retain their patients primarily lack in this important quality that is one of the characteristics of successful practitioners.

Personality

Different patients behave differently in a therapeutic relationship. Some are humble, reserved and poor in expression others are assertive, friendly and expressive; some are emotional, get upset easily, and remain tense while others are emotionally stable, and remain calm and composed; some are demanding, attention seeking, manipulative and casual in following and complying to instructions while others are sober, non-demanding, attentive and meticulous in complying to the instructions. All such differences in different patients can be attributed to the differences in their personalities. If a doctor is able to assess the personality of his patient he can predict the patient's behaviour and intervene or respond accordingly. Such an understanding does not only make the therapeutic relationship more effective but can also save the doctor from troubles inherent in dealing with "difficult" patients (Box 3). It is therefore recommended that all doctors should be able to assess personality of their patients[21].

Box 3. An example of a patient with Narcissistic Personality

"A partner in a prestigious law firm was admitted to the specialized endocrine service of a teaching hospital for investigation of inflammation of the thyroid gland. The patient had sought consultation with the chief of the endocrine service after seeing the endocrinologist's recent research findings reported on network television and characterized as glamorous, high-technology innovation. The patient recalled thinking at the time, "Finally, here is a doctor who can understand the complexities of my illness!"

When the patient arrived at the endocrine services, he was greeted by the junior resident, who introduced himself and explained that he would be responsible for the patient's day to day care, while the chief of the service would consult on major diagnostic and treatment issues. The lawyer flew into rage and shouted, "No damn wet-behind-the-ears student doctor is going to lay a hand on me!"

The resident attempted to calm the patient and agreed to ask the chief of the service to mediate the dispute. When the chief arrived and was informed of the situation, his previous experience in dealing with the influential patients enabled him to grasp the nature of the lawyer's narcissistic rage, the underlying sense of entitlement and fear that motivated it, and the embarrassment of the resident who was the unwitting target of the tirade. He welcomed the patient and apologized for not being able to meet him at the time of admission. He introduced the resident as "one of our brightest young colleagues - we are expecting great things from him" and continued, "He and I will work closely together to get to the bottom of your problems."

The lawyer was reassured by this respectful apology and the statement of confidence in the junior resident. The chief of the service had in effect transferred his reputation of excellence to his younger colleague ("passed the baton") and had thereby imbued the resident with the charismatic healing qualities the narcissistic patient needed in order to feel the trust necessary for a successful therapeutic relationship with the health care team."

Reproduced from: Marmar CR. Personality disorders. In Goldman HH ed. Review of general psychiatry, 3rd ed. Lange 1992.

Beliefs

Beliefs are views, opinions, ideas, and faith a person possesses. Broadly speaking they constitute a person's view about life on the basis of which he interprets things happening around him and makes day to day decisions. Every person has a set of beliefs that are an expression of his sociocultural, religious, ethnic and family background modified by his education, knowledge, experience and general awareness.

Like any other person, patients have their own beliefs about health and illness. These beliefs partly determine what a person does to maintain his health, the way he interprets his symptoms, and the way he seeks and sticks to a professional help when sick. To understand patients' point of view and to practice therapeutics rationally and effectively it is, therefore, essential for a doctor to have insight into patients' beliefs.

On many occasions, patients' beliefs about health and illness related matters are likely to be in conflict with the scientific principles of medicine and therapeutics. It is not uncommon to come across patients who have peculiar views about various foods, who have bizarre explanation for their symptoms, who had been to faith healers for possible cure, and who have misconceptions about various diagnostic techniques and forms of treatment. It should be realized that the beliefs of a patient are as valuable to him as your beliefs are to you. These patients, therefore, should be approached in a nonjudgmental manner and they should never be refuted, confronted or ridiculed for having such beliefs. Instead, conveying to the patient that his beliefs have been followed and are respected is definitely more beneficial in a therapeutic relationship. This expression of understanding can help develop a better rapport with the patient and establish a relationship conducive for open discussion. By such a relationship the doctor can attempt to modify and correct the patient's erroneous beliefs in an authoritative manner but in a friendly and comfortable background.

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Chapter 3

Specifying The Therapeutic Objective And Interventions

After the patient's problem has been understood in his context, the next step in rational therapeutics is to specify the therapeutic objective and define the interventions by which the objective is to be achieved. If a doctor is not clear what exactly he wants to or can achieve therapeutically, and has not communicated the desired objective to the patient, his therapeutic endeavor is likely to end up as disappointing both for himself and the patient on many occasions.

While specifying the therapeutic objective and planning the interventions two important facts are likely to be overlooked by doctors resulting in an unrealistic and irrational approach towards the problem. These two facts are:

1. All diseases are not completely curable.
2. Therapy does not mean use of medicines only.

All Diseases Are Not Completely Curable

Different diseases differ from each other with reference to their aetiology, and pathogenesis, and consequently in their natural course, intensity, and the suffering they give to a patient (and his family). It always has been human desire and effort to develop means and methods by which disease related suffering can be controlled or ideally the disease process can be arrested and reversed. Recent technological and scientific efforts in medicine also aim at achieving this but the situation, in spite of all the advances, is far from ideal. We still or confronted by many diseases that are not completely curable i.e., their disease process cannot be completely arrested or reversed.

There is a wide range of diseases with reference to their curability by any form of therapy. At one end are diseases that are self limiting even without any active therapy (if secondary complications do not occur) while, the course of those at the other extreme cannot be changed by any available form of therapy and only symptomatic relief is offered. In between are diseases that are completely or partially curable with treatment (Table 1).

Table 1. Spectrum of diseases with reference to their curability.

Curability	Examples
Self limiting	common cold, viral diarrhoea in children,
Completely curable	most infections and infestations, nutritional deficiencies
Partially curable	migraine, essential hypertension, NIDDM, some osteoarthropathies, some malignancies,
Not curable	most of osteoarthropathies and malignancies, schizophrenia, IDDM, Alzheimer's disease,

This varying degree of curability for different diseases results in a range of diseases with reference to their clinical course as well. Some diseases have a clinical course of few days to few months, if proper therapeutic interventions are made and complied to, while others do not remit with any available form of therapy and require a life long control with treatment.

Because of the above mentioned differences in different diseases, the therapeutic objective - cure, control, or symptomatic relief - also differs for different diseases. To practice therapeutics rationally, the therapeutic objective, and the time that will be required to achieve it, should always be defined from the outset. While defining the objective it is important to be realistic in approach and admit the limitations of medical science and therapeutics. Whatever is therapeutically achievable should be clearly and repeatedly communicated to the patient (and his family members) and any unrealistic expectations held by him (them) should be moderated.

Doctors usually are aware of the clinical course of the diseases they come across in their practices but they tend to overlook this important step of rational therapeutics due to different interrelated reasons:

Psychological denial of limitations

Every human has a tendency to psychologically deny his personal (and professional) limitations and the same is true for doctors. Doctors, specially those new in the profession, are likely to feel helpless and frustrated when managing a patient with an incurable illness. Because it is psychologically painful for a doctor to think about the poor prognosis of an illness, he is likely to "push" this fact into his subconscious and just not bother about it; a doctor who readily informs a patient of acute tonsillitis "do not worry about it, you will be fine within a couple of days" may not even comment on the prognosis when dealing with a patient of osteoarthritis. Because of the same psychological reason doctors are likely to avoid diagnosing conditions with poor prognosis. On the contrary, as it is consoling for a doctor to make a diagnosis which is amenable to therapy, there is a very real risk for a doctor to diagnose conditions for which therapy is available[1].

Confounding professional limitations with personal incompetence

Some doctors are unnecessarily sensitive about the therapeutic limitations of their profession and view these limitations as their personal incompetence. Such doctors fear that by admitting that a disease is "not curable", they will be considered incompetent by the patient and his family members. They, therefore, in spite of knowing the poor prognostic facts of an illness do not convey them to the patient.

Meeting patients' expectations

Because modern medicine can prevent or cure more diseases, patients often expect better results than a doctor can deliver[2]. Doctors have a tendency not to appropriate such unrealistic expectations of patients and conceal the prognostic facts due to different reasons.

Some doctors find it difficult to correct patients' unrealistic expectations because they believe such a correction can disappoint the patient and lead him to switch over to a doctor who can substantiate his false hopes. This practice, though is a form of patient manipulation and has no ethical grounds, is a socio-professional reality.

Others avoid telling the therapeutic facts to a patient as they fear that patient can go into a state of despair and hopelessness and loose interest in his treatment altogether. The reason seems to be valid because it takes patients' interest into account but is not permitted by the rules of medical ethics in most instances. Doctors have the privilege (referred to as Therapeutic Privilege) and are justified to withhold information from a patient *only* when the patient is unusually sensitive, anxious or emotional. A general policy of not disclosing information because of the presumed hypersensitivity of patients is not an acceptable basis of this privilege[3].

After it has been established that the patient should be informed about therapeutic facts, it needs to be emphasized that it is essential to psychologically prepare the patient and his family members before they are informed of the facts.

Consequences of concealing prognostic facts

Concealing the prognostic facts from patients is not justifiable no matter how divine the intentions are and in many countries it is legally not permissible. Important detrimental consequence of concealing prognostic facts from a patient are:

1. Because of his unrealistic expectations, the patient will continue utilizing his resources to achieve the un-achievable. Finally when he will learn the facts, he is not only more likely to go into despair and depression but may also curse the doctor who concealed the facts and made him spend unnecessarily.

2. When a doctor conceals therapeutic facts of a partially controllable illness from the patient, he tries to satisfy the unrealistic desires of the patient. During this

process, he is quite vulnerable to make irrational therapeutic decisions. For example, a patient of advanced rheumatoid arthritis, who has not been told that he will have to tolerate some residual pain, will expect an absolute pain free state. To meet thi expectation of the patient, the doctor is likely to prescribe analgesics in all sorts of odd and irrational combinations.

Therapy Does Not Mean Use Of Medicines Only

Another important fact to be born in mind while defining a therapeutic intervention is that therapy does not necessary mean use of medicines. Over the last few decades there has been tremendous development in the field of pharmacotherapy and now hundreds of compounds are available for use in different ailments. The progress has definitely been a milestone in the field of therapeutics but it has also given rise to some problems. One of the important problems is that medicines are over-relied upon, both by doctors and patients, to maintain or regain health.

The word therapeutics is derived from the word therapy which means any treatment, remedy, or intervention to cure or control illness. During the last few decades the pharmaceutical industry has communicated the message - a pill for every ill - so widely and effectively that the word therapeutics has become strongly associated with medication and both are erroneously considered synonymous.

While making a therapeutic decision one should not act like a computer, programmed by the drug industry or the patient, or be limited by ones own rigid views of reflex drug-giving[4]. Instead, it should always be born in mind that drug therapy, though the most commonly employed form of therapy, is not the only type of therapy; and the limitations of drugs must be understood if they are to be used well[5]. Some other well known and effective forms of therapy are surgery, physiotherapy, psychotherapy, and radiotherapy. Dietary control, weight loss, modification of personal habits, change of the environment, or rest suggested for therapeutic purposes, or simple reassurance given with a therapeutic consideration can be equally important forms of therapy in some situations. The role of these different therapeutic interventions has long been recognized and their significance cannot be overemphasized. According to Hippocrates:

> *"It is not enough to do what we can do; the patient and his environment and external conditions must contribute to achieve the cure".*

Defining the form of therapy

As mentioned above, therapy does not only mean drug therapy and any intervention that can cure or control an illness is a form of therapy. While defining the form of therapy for any disease it is logical to review all the possible forms of intervention and move from simple forms of therapy to more complicated ones while making the

choice (Table 2). There is no rationale of selecting a complicated or expensive therapeutic regimen when the desired objective can be achieved by a simpler and cheaper mean. However, it is important to realise that delay should never be made in initiating a therapy higher in the hierarchy at the expense of patient suffering or when such a delay can result in complications.

Table 2. Different forms of therapeutic interventions.

Type	Examples
Simple reassurance	For self limiting conditions, for minor and vague symptoms of psychogenic origin.
Modification of personal habits	Exercise and weight reduction for hypertension and diabetes mellitus, abstinence from tea for benign insomnia
Modification of environmental factors	Transfer to a job of lesser stress for a patient of IHD or tension headache
Use of medication	Antibiotics for infections, analgesics for pain, antihypertensives for hypertension
Other specific therapies	Surgery, physiotherapy, psychotherapy, and radiotherapy; and referring the patient.

These different forms of therapy are variously employed by doctors to treat different ailments but regretfully medicines are generally over-relied upon by most doctors. Not infrequently they are suggested for conditions for which simpler forms of therapy can be equally effective and more safe. Some common example are:

- Simply reassuring and advising a nutritious diet and rest might be enough for patients of common cold or some other upper respiratory tract viral infections, but frequently they are prescribed a list of drugs including antihistamines, decongestants, antipyretics, and sometimes even antibiotics.

- Alteration in dietary habits and exercise will benefit an obese person with mild NIDDM and offer him some protection against the diabetes associated complications as well, but he may be prescribed medication on many occasions.

- Restricting smoking, limiting intake of tea and encouraging exercise will help a patient of benign insomnia, who may end up with dependence on benzodiazepines, originally prescribed to him by a doctor.

- An elderly undernourished person with chronic constipation may be spending money on laxatives suggested to him by a doctor, whereas a high fiber diet can be equally effective and definitely of more nutritious value then laxatives.

- A house wife with vague stress related multiple bodily symptoms may be prescribed a list of drugs for symptomatic relief while she can benefit equally by an attentive listening and reassurance.

In many instances maximum benefit can be offered to a patient by using different forms of therapy in combination. For example, in addition to medication, surgical drainage of an abscess will be necessary to control an infection, postural drainage will speed up recovery of a patient of bronchiectasis having superimposed infection, steam inhalation will benefit a patient of acute sinusitis, physiotherapy will offer additional benefit in certain cases of rheumatic pain, and dietary control and exercise will be helpful for a patient of NIDDM or hypertension. In such situations relying only on medications can result in delay in recovery, prolong patient suffering and the duration of treatment, give rise to complications, and result in increased financial burden on the patient. Whenever a combination of therapies is deemed to have added therapeutic benefit, all of them should be suggested to the patient and effort should be made that patient complies with all of them.

An important practical consideration while selecting a therapeutic intervention is to take care of patients' convenience. The aim should always be to select a therapy or combination of therapies that offer maximum benefit to the patient but minimally incapacitate him personally, socially, or financially. For example:

- A patient with mild non-insulin dependent diabetes mellitus who can comply with dietary restrictions and a weight reduction program may be given a trial of therapeutic dietary restriction and exercise but another patient of diabetes mellitus of the same type and severity, who clearly is unable to comply to such restrictions due to his personal or social reasons, may require treatment with medication.

- A patient of allergic rhinitis, who works as an office assistant and use public transport for transportation can safely be prescribed conventional antihistamines, but a taxi driver with the same condition will be needing non-sedating antihistamines if he desires to continue his job.

- A depressed financially well-off businessman may be advised a non-sedating antidepressants (costing him up to Rs.80 a day), but for a depressed labourer a tricyclic antidepressant will be an appropriate choice (costing him less than Rs.30 a day).

Referring the patient - a type of therapeutic intervention

It is not possible for any doctor to have all the knowledge, skills, training, and technology to effectively treat all the patients visiting him/her. In situations, where a doctor realizes that he does not possess the expertise to evaluate or treat a patient,

the help he can offer is to refer the patient to an appropriate doctor. The same is his moral obligation as well.

In addition to the above mentioned situation, there are two others in which a patient should be referred to some other doctor[6]:

1. When progress is hindered by personality conflicts between the doctor ant patient, and
2. When progress is hindered because dependency between patient and doctor is so binding that they cannot work effectively together (referred to as detrimental dependence).

Helping a patient, therefore, does not always mean using one's own resources to treat a patient. Rather, in some cases it may mean knowing when and where to refer the patient for further evaluation and treatment.

Defining therapeutic intervention when diagnosis is uncertain

The discussion so far focused on how to define a therapeutic objective and make necessary interventions after a diagnosis has been established. In practice there are many occasions when doctor is uncertain about the diagnosis and, therefore, he exactly does not know how to intervene. A usual objective of doctors in most such situations is to make the patient free of symptoms, which is commonly achieved by one of the following means:

Treating all the probable diagnoses concomitantly

Not infrequently doctors are confronted by a situation in which they have reached a list of probable diagnoses but are unable to conclude a single diagnosis with certainty. The situation is quite tricky, specially when investigations cannot be carried out due to some reason or when they also have not yielded anything conclusive.

Doctors generally approach such a situation by starting treatment for all the probable diagnoses simultaneously. It is not uncommon to see patients of febrile illness receiving antimalarials and antibiotics concomitantly (Prescription 1), patients with a psychiatric illness taking antidepressants and antipsychotics simultaneously, and patients with skin problems applying steroid and antifungal preparations at the same time. The practice makes sense when it is carried out in complicated and confusing situations, but if carried out as a routine it indicates doctors incompetence and lack of effort, and is not justifiable. Therapy for two or more than two tentative diagnoses should only be initiated after a sincere effort to reach a single diagnosis has proved inconclusive.

Mr. Malik M. Ramzan   Date 07-9-1996

Cold +++ 2 Days P/C all on [illegible] Th.

Ry. [illegible] O/E Throat Congested. Rhin...

1. Tab. Fansidar (3) [illegible]
2. Tab. Panadol E (20) 1+1+1+1
3. Cap Minocin 100 (10) 1+1
4. Tab Sherlef (1) [illegible]
5. Tab Nivaquin (10) 1+1+1

PRESCRIPTION 1. Antimalarials (Fansidar and Nivaquin) and an antibiotic (Minocin) given together - An example of diagnostic uncertainty.

Treating the symptoms

Sometimes patients present with vague somatic and psychological complaints that do not fit into any specific diagnosis. These vague symptoms are generally believed to be an expression of psychological stress and are more frequent in females. The situation is specially common in primary care and general practice settings where, according to some estimates, 50% of all visits are motivated by or are manifestations of psychological or emotional problems[7].

A common approach towards such patients is to offer them symptomatic treatment, and sometimes a long list of medicines need to be prescribed to achieve this (Prescription 2). The approach, generally speaking is not quite rational. Instead, effort should be made to dig down to find the basis of these symptoms. If symptoms are an expression of psychological stress, then the best therapeutic approach is to reassure and, if possible, counsel the patient. If they seem to be a presentation of some psychiatric illness, the illness should be properly treated or the patient should be refereed to a specialist for care.

Therapeutic trial - a method to establish a diagnosis

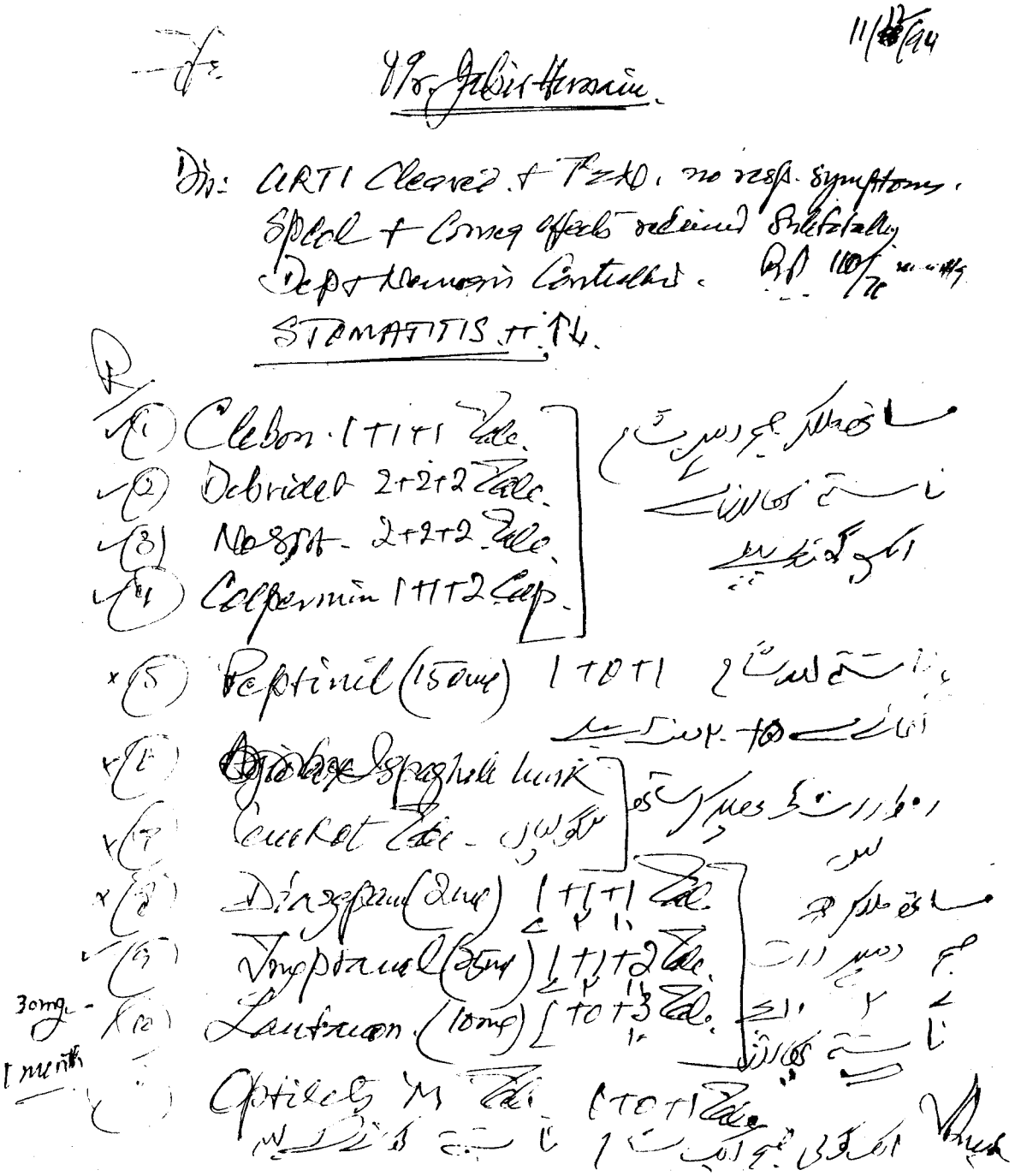
Sometimes the situation of uncertainty over diagnosis is tackled by doctors by offering the patient a "therapeutic trial". During a therapeutic trial the patient is prescribed treatment for the most likely single diagnosis. If the patient responds to the suggested treatment, the diagnosis gets confirmed, otherwise it is rejected. Epilepsy and tuberculosis are two common conditions where this approach is usually employed; some doctors also approach an undiagnosed febrile illnesses in the same manner (e.g., they will prescribe antimalarials first and if the patient does not respond within a day or two then they will add an antibiotic to the treatment). Of the commonly used methods to handle the situation of uncertainty over diagnosis, this method appears to be the most rational.

Factors adversely effecting the choice of therapeutic intervention

(Factors that influence the prescribing pattern of doctors are discussed in section 2 of the book in detail. Here, a brief review of factors adversely effecting the choice of therapeutic intervention is provided just to maintain the continuity).

Rapid relief of symptoms

Patients desire to be rapidly relieved of the symptoms of illness. The desire is understandable - symptoms are a source of distress. Some patients also desire a rapid relief because they cannot afford a lingering on sick role due to personal, social, or, more importantly, occupational and financial reasons. Patients, therefore, tend to



PRESCRIPTION 2. Polypharmacy. Polypharmacy may be the result when a physician unnecessary relies on drugs, is uncertain about diagnosis, or is attempting to offer symptomatic relief.

prefer a doctor who can relieve their symptoms rapidly. When a doctor attempts to achieve this, he is likely to select an inappropriate therapeutic intervention.

Easy to suggest, easy to follow

Patients generally prefer to be advised a regimen that is easy for them to follow; and their is no regimen easier than having a few tablets swallowed a few times a day. While complying to such a desire of patients, doctors are likely to avoid suggesting other therapeutic interventions of equal, and sometimes, even of more importance.

Similarly some doctors, just to avoid the effort of educating and convincing the patient, resort to advising a regimen that is easy to suggest. And in a social set-up where patients convincingly expect drugs to be prescribed, nothing is easier to suggest than drugs.

Patient's expectations

Patients are eager to take medicine[8]. They see medicines as a key to health and expect to be prescribed a medicine whenever they visit a doctor. In a therapeutic setting, the train of thought for both the patient and the practitioner is simply - you get sick, you see a doctor, nurse or pharmacist, he prescribes a medicine (or more often several medicines, at least one of which should be an injectable) and you are made well again[9]. People not only believe that drugs are a solution for any health problem but also hold the opinion that expensive drugs must be better than the cheaper ones[10]. In an attempt to fulfil these expectations of patients, doctors are likely to prescribe medicines (in many instances the expensive ones) for conditions in which none is needed, and forego non-medicinal interventions when required.

Poor knowledge in pharmacology and therapeutics

Development in the field of pharmacology and therapeutics is quite fast and new drugs are continuously being introduced in the market. The number of drugs for which a doctor has never received any formal education goes on increasing with every year of his practice. According to American College of Physicians, "approximately 85% of all prescriptions written by senior physicians who graduated from medical school in 1960s will be for a drug about which they have received no formal education[11]".

The situation demands that the doctors make an effort to keep themselves updated about the advances in therapeutics. Because the circumstances generally are not much conducive for such an academic effort, doctors tend to rely on the information provided to them by the pharmaceutical industry. The information is biassed and by relying on it doctors are likely to make inappropriate therapeutic choices.

Uncertainty over diagnosis

When a doctor is not certain about diagnosis, he is likely to approach the illness by hit-and-trial method or resort to symptomatic treatment. The method is inappropriate and always needs to be avoided. A better and a rational approach is either to make an effort to establish a diagnosis and treat it accordingly or to refer the patient to someone deemed to be an expert in handling the situation.

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Chapter 4

Therapy With Drugs

A drug is "any chemical agent that effects processes of living[1]". It is "any small molecule that, when introduced into the body, alters the body's function by interactions at the molecular level[2]". This definition of drugs embraces poisons as well; the difference only is the way a drug is administered or the intent with which it is administered. As a drug administered with criminal or suicidal intent is a poison, similarly a drug administered injudiciously can prove toxic or poisonous. Since doctors play a strategic role in the use of drugs, they are ethically obligated to ensure that they do not suggest their use in a careless or irrational manner.

The problem of irrational prescribing

The revolution of "treatment with drugs" that began during World War II has advanced rapidly over the last 50 years and is responsible for what has been called "the drug explosion". This "explosion" has provided us with hundreds of compounds for use as medicines, and now, drug therapy is the most widely used form of therapy. One of the consequences of the availability of so many drugs is that they are prescribed and used inappropriately, unnecessarily and irrationally, and such an undesired use of drugs is now a recognized global problem. Numerous studies, both from developed and developing countries, show that prescribing practices are frequently illogical, irrational, and even dangerous[3]. The common irrational prescribing patterns include polypharmacy, the use of drugs of poor therapeutic value, the use of drugs that are not related to the diagnosis, the unnecessary use of potent drugs, the inappropriate use of antibiotics, and use of unnecessarily expensive drugs[4,5]. This irrational and inappropriate use of drugs is a matter of major concern for both the developed and the developing countries, as has been recognized by the World Health Organization[6]:

> *"In developed countries inappropriate and unnecessary prescribing is placing a severe strain on the health care budget as well as increasing the burden of iatrogenic disease. In developing countries the unnecessary use of inessential medicines and the relatively high cost of many essential ones impedes the delivery of health care. Irrational drug use is therefore a matter of major concern for all countries".*

Prescribing is a complex process which is both highly individualized and dynamic and which, in addition to doctor's therapeutic knowledge, is subject to social, cultural, and marketing forces[7]. Therefore, numerous factors contribute to the problem of irrational prescribing. A textbook of pharmacology comments on the irrational use of drugs and factors contributing to it as follows[8]:

> *"Medicine has made great strides since Voltaire's satiric description of physician as "men who prescribe medicine of which they know little, to cure disease of which they know less, in human beings of which they know nothing." And yet, the profession currently remains in danger of irrational and irresponsible therapeutic practices. Physicians are characteristically rational and responsible, but it is nearly impossible for them to appear so if they respond to the pressure of time, uncritical reading, industrial advertising, and the persuasion of "detail men" and patients to use the flood of new drugs without proper education in therapeutics and without sufficient knowledge about or rational expectations of each drug."*

Rational approach to drug therapy

Before doctors prescribe a drug, they should make up their minds on several points. These include deciding whether they should interfere with the patient at all; what alteration they might hope to achieve; whether the drug they have chosen is the best to bring it about; and whether the likelihood of benefit, by treatment with drugs, overweighs the likelihood of harm[9]. To serve the best interest of the patient, and the society at large, a doctor is supposed to make all these decisions on the bases of scientifically established facts in a logical and rational manner.

Rational prescribing consists of selecting the right drug for the right patient in the right amounts at the right times. To practice rational prescribing a physician has to exercise good clinical judgment and follow scientific principles. He has to weigh the advantages and disadvantages of alternative treatment choices and select a therapy that is safe, effective, and cost-effective for the situation under consideration. He also has to decide for the most appropriate dosage form and duration of therapy, and has to monitor the treatment for potential side effects, the possibility of drug interactions, and the therapeutic results. But before making all these decisions regarding the use of drugs, physicians need to see whether therapy with drugs should be suggested in the first place.

Is therapy with drugs really necessary?

During the last few decades drugs have achieved a status of an "essential commodity" to regain and, in some instances, maintain health. Being dazzled by the relatively few really effective products that have emerged during the last 50 years, we have not

remained sensible about the use of drugs; we do not recognize their limitations, use them too frequently and expect that they could provide an answer to all our ills[10].

Sometimes the most appropriate therapy does not require drugs[11] but doctors still prescribe them for control or cure of the illness. They tend to believe that drugs are the only solution to an illness and are likely to suggest for conditions that are self-limiting or that can be cured or controlled even without them. Patients also believe the same and expect to be prescribed drug/s whenever they consult a doctor. As mentioned in the previous chapter, the train of thought for both the patient and the practitioner is simply - you get sick, you see a doctor, nurse or pharmacist, he prescribes a medicine (or more often several medicines, at least one of which should be an injection) and you are made well again[12]. In this scenario of beliefs and expectations doctors are vulnerable to prescribing drugs even when none is needed.

While prescribing drugs it is important to judge the risk of a drug against its benefits[13]. If the therapeutic objective can be achieved without drugs or if the disadvantages of drug therapy, whether medical, financial or social, are greater than its advantages, then a sensible approach is not to prescribe drugs. Similarly, there is no rationale in resorting to drugs for treatment of conditions that do not have any scientifically established form of drug therapy. To be a rational practitioner, physicians, therefore, have to know when not to resort to drugs and how to convince their patients on those occasions that it is in their best interest to abstain from drugs[11].

Prescribing a rational drug in a rational way

After it has been logically and scientifically decided that a patient needs a drug for any specific illness the next step is to select a rational drug in a rational way. A rational drug is a drug that is safe, effective, suits the patient and is cost-effective. And rational prescribing refers to prescribing that takes account of safety, efficacy, appropriateness, and economy.

Safety

Every drug, because of its pharmacokinetic and pharmacodynamic characteristics, has effects that are therapeutically undesired and so are referred to as undesirable or side effects of that drug. Safety of a drug is a measure of these side effects; obviously, a drug with fewer and/or less severe side effects is safer than a drug with severe and/or more side effects. Since treatment decisions always involve some degree of uncertainty about the beneficial and harmful effects of alternative treatments, these effects should be discounted by their probabilities (to the extent that they are known) in calculating the expected utility of various treatment alternatives[14].

A prescriber has to be well aware of the side effects of the drugs that he prescribes or frequently comes across. The knowledge about the side effects of the drugs will not

only help him to prescribe a drug that is safe for a patient, it would also ensure that he does not miss a symptom of the patient heralding some serious side effect of the drug. For example, inability of the physician to relate the tremors and palpitation of a patient on antidiabetic therapy to possible hypoglycaemia, and the sore throat of a patient on carbamazepine therapy to possible agranulocytosis, and make interventions accordingly, can be of fatal consequences to the patient. Similarly, physician's awareness of the side effects of the drugs can save the patient from unnecessary suffering and inappropriate therapeutic interventions on many occasions. For example, it is not uncommon to see patients receiving propanolol or methyldopa being prescribed psychotropics for their psychological symptoms that, in fact, may be side effects of these drugs and could be alleviated by simply changing the drug they already are taking.

Efficacy

Efficacy of a drug is its ability to produce the purported effect as determined by *scientific* methods. It is the maximal effect that can be produced by a drug and, contrary to the conception of many prescribers, is not synonymous with the potency of the drug. Potency of a drug is measure of its effects as related to its plasma concentration and potency of a drug *per se* is relatively unimportant in the clinical use of drugs as long as the given dose can be given conveniently. There is no justification of the view that more potent drugs are superior therapeutic agents[15]. Because effectiveness of a drug is related to the dose taken, the physicians should ensure that they prescribe drugs in the recommended therapeutic dosage, and make all possible attempts to ensure that the patient complies to it.

In view of the fact that the pharmaceutical market is flooded with preparations that are of doubtful efficacy and do not offer any clear therapeutic benefit (see chapters 9 and 15 for details), it is extremely important for doctors to be aware of the efficacy of the drugs they prescribe. Prescribing drugs of doubtful efficacy exposes patients to unnecessary side effects, is a waste of their financial resources, and results in the reinforcement of the belief that drugs are a solution to every problem. Physicians should always refrain from prescribing drugs that do not have a clearly established therapeutic efficacy, even for a placebo-effect reasons.

Appropriateness

For rational prescribing the physician has to consider the appropriateness of the drug being prescribed. Appropriateness, here, is used in a broad sense and does not only mean that the drug should be appropriate to the clinical situation under consideration. It means that the drug should be appropriate for the patient *in general*; it should minimally interfere with the daily activities of the patient, should not pose unnecessary risks to him, should be in his financial access, and should be in a form and dosage that can be easily administered by the patient. Because patients differ from each other in their individual, professional, and social characteristics a drug that is appropriate for one patient might not be appropriate for another patient of the

same illness. A treatment that is suggested to a patient without taking its appropriateness into consideration, on most occasions, proves "inconvenient" to the patient. This results in poor compliance on the patient's part and a therapeutic failure on the physician's part. Doctors, therefore, should always attempt to suggest a treatment that is most appropriate to the patient.

Cost-effectiveness

Rational prescribing also takes into account the cost of the suggested treatment. Physicians have to be aware of the prices of drugs they prescribe since, if their patients or the public health service cannot afford them, they will not be bought[11]. Prescribers aim should always be to suggest a treatment that is cost-effective. Suggesting expensive treatment when a cheaper and equally effective is available, with a plea that patients feel more satisfied with expensive treatment, is not rational. Similarly, suggesting expensive treatment to the financially affording patients, merely because they can afford it, also does not carry much rationale. Doctors also might prescribe expensive preparations even when cheaper preparations of the same compound are available with a belief that "the cheaper ones are not effective ". This, however, is not always true and a doctor should never discard a cheaper preparation simply because of this belief.

It needs to be emphasized here that cost-effective prescribing does not mean cheaper prescribing. In fact cheaper prescribing may not always be truly cost-effective[16]. The basic consideration in cost-effective therapy is to select a drug that best suits the patient and not to resort to expensive forms of treatment unnecessarily.

Knowledge about drugs and drug therapy - a prerequisite to rational prescribing

Problems in prescribing are often due to poor knowledge of drugs or understanding of the drug use process[17]. Of foremost importance in selecting a rational drug is to have a sound and competent knowledge of the group of drugs from which the choice is being made. As discussed in chapter 7, though a lot is taught about drugs in the medical college years, it is generally deemed not to be of much practical therapeutic relevance . The continued development of new pharmacological agents for which the doctor may not have received any formal education, lack of an ongoing training of doctors, and scarcity of and difficult access to unbiased information on drugs further worsens the situation.

The process of rational prescribing starts with reviewing all the drugs of the group from which the patient needs one. For such a review mere awareness of the brand names of these drugs is not enough at all. The prescriber should be well familiar with the pharmacological characteristics, both pharmacokinetic and pharmacodynamic, of these drugs. If a fixed-dose preparation is to be prescribed, it is a professional obligation of the prescriber to be aware of the ingredients of the preparation along

with the amount of each. In addition, to select a drug rationally knowledge of different forms of preparations, and their comparative efficacy, safety and cost is essential as well. The doctor also needs to have a sound knowledge about the side effects of the drug he is prescribing and how to deal with them, as well as dangers of its possible interactions with other drugs and various foods and the likelihood of dependence on it. Considering the rapid pace of progress in the field of pharmacotherapy, it is also important for doctors to keep themselves abreast of recent advances in pharmacotherapy. This, however, does not mean that they should rush to use the newer drugs. Instead they should start using them only after they have been convinced of their superiority over the existing forms of therapies, after thoroughly going through the objective information regarding them.

Difficult access to objective information on drug therapy

Therapy with drugs can be considered one of the scientific revolutions of the century. Starting with the discovery of Penicillin in 1920s, thousands of compounds have been tested for use as medicines and hundreds of them are now available for use in humans. New drugs are constantly being introduced into the market and, with the passage of time, more is being learnt about the existing drugs. It has been estimated that approximately 20 new drugs get introduced each year. Drugs are the primary therapeutic weapon of doctors, who have the ethical responsibility of selecting the most appropriate treatment for their patients[18]. Therefore, it is extremely important for doctors to keep themselves up-to-date about drugs.

Information about drugs and pharmaceutical products is a prerequisite to ensure proper utilization of drugs and the practice of rational prescribing[19]. But often the choice of drugs by doctors in the developing countries is inappropriate because they have little access to balanced and complete information. The situation becomes even grave when the doctors uncritically accept the information provided by the manufacturers, who usually emphasize the advantages and soft pedal the disadvantages of their products[20].

After the completion of formal medical college and house officer training, there is no systemic exposure to intelligent, informative, and unbiased assessment of drug therapy. Doctors, specially those not working in the teaching institutions, face the problem of keeping up-to-date in therapeutics[17]. Continuing "education" in pharmacology occurs as the result of random encounters with a variety of information sources, including medical journals, interaction with colleagues, and pharmaceutical industry sales representatives. The entire process can be characterized as largely random, incomplete, and subject to distortion[21]. The difficult access to unbiased and objective information about the advances in therapeutics is recognized by the World Health Organization as follows:

> *"Whereas the cumulative of expansion of the scientific medical literature is prodigious and much of this is related to drug therapy, little of this output directly influences the prescribing practices of doctors. The original literature is*

largely inaccessible to the busy generalist and over the past two decades an appreciation has developed that greater efforts are needed to provide prescribers with readily assimilated, independent and objective information that will keep them adequately informed of changes in therapeutic practice throughout their professional careers[22]."

Sources about drug information

To effectively and rationally select a drug for a patient, physicians' need for objective, concise, and well-organized information on drugs is obvious. Among the available sources are textbooks of pharmacology and therapeutics, medical journals, drug bulletins, drug formularies, drug compendia, professional seminars and meetings, symposia, advertising, and drug information material provided by the pharmaceutical industry. Despite this cornucopia of information, responsible medical spokesmen insist that most practising physicians are unable to extract the objective and unbiased data required for the practice of rational therapeutics[23].

Pharmacology textbooks provide basic pharmacological principles, critical appraisal of useful categories of therapeutic agents and detailed description of individual drugs. But obviously these do not contain information on the most recently introduced drugs that are usually in common use. The viewpoint offered in these textbooks is usually that of the hospital-based consultant and applied aspects of therapeutics are discussed superficially[24]. Similarly, most **textbooks of medicine** are also of limited benefit; they usually discuss therapeutics superficially and do not provide information about the recently introduced therapies. Additionally, most of these books are written by authors from the developed countries and lack the perspective of the developing world. The textbooks written for post-graduate use, particularly if they are frequently updated, should offer a reliable distillate of existing knowledge on a given topic but it is an overwhelming task for the editors, no matter how highly motivated they are, to keep abreast of current therapeutic information in an authoritative and comprehensive manner.

Medical journals can be of help in remaining up-to-date about various advances in pharmacotherapy and therapeutics but a great many of them are industry sponsored and, as such, are not seen as unbiased[18]. In these industry sponsored journals specific drugs are prominently and favourably described and the information they provide cannot be relied upon. Journals that are not industry sponsored and provide an objective and unbiased information are few and among others include: *Clinical Pharmacology and Therapeutics, Drugs, New England Journal of Medicine, Annals of Internal medicine, Journal of American Medical Association, Archives of Internal Medicine, British Journal of Medicine, Lancet,* and *Postgraduate Medicine.* These journals are a good source of original and objective information. But they are expensive, have to be subscribed, are usually available in the libraries of teaching hospitals only, and therefore, are not in easy assess of most of the practitioners.

Drug bulletins are periodicals that are concerned with the promotion of rational drug therapy and appear at frequent intervals, weekly to every three months. They provide assessment of drugs and practical recommendations about their use. The drug bulletins commonly referred to are Drug and Therapeutics Bulletin(UK), and Medical Letter(USA).

Drug bulletins are an essential tool for keeping abreast of developments in the field of drugs. But they are also not in easy assess of most practitioners. In addition, the information in drug bulletins is often drawn largely from international sources and, as such, this is sometimes of questionable priority - or even relevance, to local needs[24].

Drug formularies contain a list of pharmaceutical products that have been approved by a body of experts. They are developed by special committees comprising of physicians and pharmacists, and indicate drug products that are approved for use in specific health care setups. They generally do not provide information on the drugs they contain.

Information provided by the pharmaceutical industry in the form of direct-mail brochures, journal advertising, professional courtesies, or the detail person or pharmaceutical representatives is intended to be persuasive rather than educational. Information provided through these sources is freely and easily available but frequently it is biased; positive aspects of the product are often emphasized, while negative aspects are overlooked or given a scant coverage. This is something to be expected. The underlying purpose of medical information, particularly data on therapeutics, provided to physicians from commercial sources is, understandably, to promote product sales. Although information from these sources may also promote useful awareness and understanding of therapeutics, the primary purpose of medical information from these sources is not to supply a balanced, unbiased, or objective view of scientific data. The pharmaceutical industry cannot, should not and indeed does not purport to be responsible for the education of physicians in the use of drugs[25]. Therefore, in all instances where medical information is provided to physicians under commercial sponsorship, physicians are ethically obligated to recognise the potential bias inherent in it (see chapter 8 for details).

The source of information most often used by physicians are **drug compendia**. Quimp and Pharmaguide are the most widely used compendia in our country. Both these only list the compounds and drugs available in the market, describe their uses, as indicated by their manufacturers, enlist their side effects, and provide the prices of these drugs. The information is identical to and in most instances even lesser than that provided on the insert pack of a product. Because comparative data on efficacy, side effects, and general prescribing instruction is not included in these compendia, they have a very limited usefulness in providing information necessary to practice therapeutics rationally.

Choosing between the sources of information:

The practising physician's primary obligation is toward the patient. To fulfil this responsibility physicians must ensure that their selection of therapies is based on the best, objective information[26] The best clinical practice depends, over time, on such objectivity.

To prescribe rationally, it is necessary not only to have speedy access to objective information on drug efficacy, safety and quality but also to use that information correctly. Prescribers, therefore, have to be capable first of judging if the information available to them is objective (Box 1), then of selecting an appropriate drug in the right dosage form in the light of that information.

Choosing between the sources of drug information is an important step when deciding on how to keep up-to-date. The ultimate goal is to solve a patient's problem effectively in clinical practice. The advantages and disadvantages of various sources of drug information have been outlined above. Textbooks are of help in remaining in touch with the basics of therapeutics. They can also be consulted by a physician when he is in doubt about a clinical situation and the required therapeutic interventions. Medical journals that are not published by the pharmaceutical industry, and drug bulletins are a good source of unbiased and objective information about the advances in the field of therapeutics.

In the absence of any formal ongoing training of doctors, the pharmaceutical industry is an important source of information about drugs to doctors. Doctors tend to rely heavily on this information, which in most instances is promotional and nonscientific. Because of the bias inherent in the information provided by the industry, reliance on it can lead the physicians to adopt inappropriate and irrational prescribing habits. It has been demonstrated that those doctors who obtain their prescribing information from pharmaceutical sources are less rational prescribers than those who obtain such information from colleagues[18]. The predominance of commercial rather than scientific sources of drug information, therefore, has been identified as a problematic area in health care delivery[27]. To fulfil the responsibility of effective patient care and rational prescribing, physicians need to realize that they are naturally susceptible to the persuasive actions of commerce[26]. They should not rely on the information provided by the industry and, as recommended by WHO, any information provided through these sources should not be used in isolation from other more objective sources[28].

Are newer drugs always better drugs?

Developing a new drug is not cheap. The Pharmaceutical Manufacturer's Association estimates that to bring a new drug from discovery to market requires an average of 12 years and $231 million. It is, therefore, no wonder that the pharmaceutical manufacturers invest both time and money in vigorously marketing their products both to physicians and the public[29].

Box 1. Efficient reading

Articles

Many prescribers have a problem reading anything they would like. The reasons are lack of time and - in industrialized countries - the sheer volume of materials mailed to them. It is wise to adopt a strategy to use your time as efficiently as possible.

You can save time when reading clinical journals by identifying at an early stage articles which are worth reading, through the steps listed below.

1. Look at the **title** to determine if it appears interesting and useful to you. If not, move on the next article.
2. Review the **authors**. The experienced reader will know of many authors whether they provide valuable information or not. If not, reject the article. If the authors are unknown, give them the benefit of the doubt.
3. Read the **Abstract**. The main point here is to decide whether the conclusion is important to you. If not, reject the article.
4. Consider the site to see if it is sufficiently similar to your own situation, and decide whether the conclusion may be **applicable** to your work. For example, a conclusion from a research in a hospital may not be relevant for primary care. If the site differs to much from your own situation reject the article.
5. Check the '**materials and methods**' section. Only by knowing and accepting the research method can you decide whether the conclusion is valid.
6. Check the **references**. If you know the subject you will probably be able to judge whether the authors have included the key references in that field. If these are missing, be careful.

Clinical trials

Few general principles on how reports on clinical trials should be assessed are given below:

Generally, only randomized, double-blind clinical trials give valid information about the effectiveness of a treatment. Conclusions drawn from studies of other designs may be biased.

Second, a complete description of a clinical trial should include: (1) the patients in the trial, with number, age, sex, criteria for inclusion and exclusion; (2) administration of the drug(s): dose, route, frequency, checks on non-adherence to treatment, duration; (3) methods of data collection and assessment of therapeutic effects; and (4) a description of statistical tests and measures to control for bias.

Finally you should look at the clinical relevance of the conclusion, not only its statistical significance. Many statistical differences are too small to be clinically relevant.

Sometimes conflicting evidence is presented by different sources. If in doubt, first check on the methodology, because different methods may give different results. then look at the population studied to see which one is more relevant to your situation. If doubts remain, it is better to wait and to postpone a decision on your drug choice until more evidence has emerged.

Reproduced from: World health Organization. Guide to good prescribing. World Health Organization Action Programme on Essential Drugs. WHO, Geneva 1995. p74-75.

In the search of new drugs, many compounds get developed that do not offer any significant therapeutic advantage over the existing ones. Not infrequently, the manufacturers bring these compounds to the market for business reasons[30]. Because these drugs do not offer any real therapeutic advance, they are frequently referred to as "me too" drugs.

Manufacturers wage aggressive campaigns to change prescribers' habits and to distinguish their products from the competing ones, even when they are virtually indistinguishable. Unsubstantiated claims of pharmacokinetic and pharmacodynamic superiority, and cost-effectiveness are made in the promotion of these drugs[30]. Typically, the initial promotion of any new drug is accompanied by extensive advertisement of its virtues - often a useful way of bringing a product to physicians' attention. However, if with continued experience the benefits are found to be lower and the risks higher for a given drug, this information is reported in the academic literature and in small print in the "prescribing information" sections of the advertisements, both places which apparently do not strongly influence physicians' knowledge about drugs[27].

Doctors are often overwhelmed and confused by the volume and content of such pharmaceutical promotion and by the lack of comparative evidence to enable them to distinguish between similar drugs or between genuine advances and "me too" drugs[17]. They quite often are attracted by the promotional claim of these new drugs and start prescribing them without any sound scientific reason:

> *"A doctor with any pretentions to being a clinical scientist might be embarrassed at the way many doctors have responded to new drugs and new innovations in the last 3 to 4 decades. All to often they have behaved like children who see new toys. They want it immediately. Very soon they discard it for another[31]."*

Though the drug manufacturers may convey the message "the newer the better" to the doctors, it is their professional obligation not to yield to this message until they have made an objective and scientific evaluation of the information regarding these drugs. Attitude toward new drugs, as suggested by a well known text-book of pharmacology, should be[32]:

> *"A reasonable attitudes towards new drugs is summarized by the adage that advises the physician to be "neither the first to use new drugs nor the last to discard the old". Only a minor fraction of new drugs represents a significant therapeutic advance. The limitation of information about toxicity and efficacy at the time of the release of the drug has been emphasized above, and this is particularly pertinent to comparisons with older agents in the same therapeutic class. Nevertheless, the important advances in therapeutics in the last 50 years emphasize the obligation to keep abreast of significant advances in pharmacotherapy."*

Evaluating information about new drugs

Whenever a doctor is interested in starting prescribing a newly introduced drug, he should be able to evaluate the information concerning it. The objective and unbiased sources of information mentioned above can be of help in this regard. A useful and systemic way to evaluate any such information is "STEP", an acronym for safety, tolerability, effectiveness, and price (Box 2). All four attributes should be considered when weighing the purported advantage of one drug over another[33].

Box 2. Evaluating information about a new drug.

One useful way to evaluate information from drug representatives (or other sources) is "STEP", and acronym for safety, tolerability, effectiveness, and price. All four attributes should be considered when weighing purported advantage of one drug over another. Safety applies to the likelihood of long term or serious side effects caused by the drug. Tolerability is best measured by comparing the pooled dropout rates between the new drug and a competitor drug, rather than trying to weigh the relative incidence of side effects. The best way to evaluate effectiveness is to compare the new drug with your current favourite. The necessary information may be hard to come by, specially since research funded by a drug company may not be published if the results show no benefit of its drug over that of its competitor. Lastly, the price of the drug should include not only its direct costs but any indirect costs, such as additional monitoring or extra visits to a doctor. So, until your drug representative produces (or you yourself are able to find and read it) valid data that a drug is at least one STEP better, you current practice need not change.

Reproduced from: Shaughnessy AF, Slawson DC. Pharmaceutical representatives - effective if used with caution. BMJ. 1996;312:1495.

Adequate knowledge alone is not sufficient for rational drug use

It seems that main reason for incorrect prescribing is a lack of knowledge and that if prescribers had the correct information, their prescribing would automatically improve. This is not always the case and adequate knowledge on rational drug use does not always result in rational prescribing behaviour[5,34-36]. An important reason for this, as mentioned above, is that prescribing is a complex process which is both highly individualized and dynamic and which, in addition to doctor's therapeutic knowledge, is subject to social, cultural, and marketing forces. A doctor may prescribe for reasons other than the pharmacological effects of a drug; he may prescribe to maintain patient contact, to satisfy a humane urge to give something to a distressed patient, to terminate a consultation, or simply because of perceived patient demand[17].

Rational prescribing, therefore, is not an easy task. The prescriber has to know a great deal about the condition, the patient, and the possible treatment alternatives to

decide how best to proceed. He should be able to approach any new information about the advances in therapeutics critically and possess the ability to assess his own prescribing habits vigilantly. He also needs to have a good understanding of factors that influence the prescribing behaviour. And most importantly, he should have a sense of responsibility towards his patients, his profession, and the society: As has been commented upon by a textbook of pharmacology[37]:

> *"It is clear that drug therapy involves a great deal more than matching the name of the drug to the name of the disease; it requires knowledge, judgment, skill and wisdom, but above all a sense of responsibility."*

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Chapter 5

Writing A Prescription

A prescription is a physician's written order to prepare or dispense a specific treatment - usually medication - for a specific patient. It is an important therapeutic transaction between physician and patient and is an indicator of physician's knowledge, clinical skills, and understanding of the patient. In addition, the general pattern of prescription writing, as observed in a country, also reflects the way physicians of that country have been trained and the regulatory effectiveness of the health services of the country.

The standard way of prescription writing

While drugs can be prescribed on any piece of paper, most of the countries have defined standards regarding the information that should be provided on a prescription. Similarly every country also has its own laws determining which drugs require a prescription, which ones may be bought (or sold) without a prescription, and who is entitled to write a prescription. Clearly these laws are well established and vigorously enforced in countries with an established and well regulated health delivery system.

Traditionally, a prescription order is written in such a way that it, in addition to providing the identity of the prescriber, identifies the patient and his problem, and provides easily interpretable instructions to dispenser and the patient. The major elements of a prescription are[1,2]:

Date

The date when the prescription is written is to be specified on a prescription order. It indicates when the patient was advised the treatment and helps the dispenser know whether the patient is using some old prescription to purchase specific drugs or has he consulted a doctor recently. He can then refuse to fill a prescription if too much time has lapsed since its writing, specially if the drugs contained on it are dangerous or have a potential for dependence. The date specified on a prescription can also help a doctor to exactly know when the patient had previously consulted him or some other doctor and for what ailment he had made the consultation for.

Prescriber's identity

A prescription is supposed to have the prescriber's name, professional degree/s, and address of his practice along with his phone number if he has one. Many countries also require prescriber's license number on the prescription which may be printed on his prescribing pad or written by him below his signatures. Doctor's identity on a prescription helps in identifying who has ordered the prescription.

Name, address, and age of the patient

A standard prescription contains the name, address, and age of the patient. These are necessary in order to expedite the handling of the prescription order and to avoid possible confusion with medications intended for someone else. In some countries the pharmacist or dispenser is to place the name of the patient on the bottle or container, as is written on the prescription.

Drugs prescribed

The body of a prescription order contains the name of the suggested drug/s. It should always include the strength of the suggested drugs along with the dose to be taken. Abbreviations should be avoided since their use frequently results in error[3]. If more than one drug is suggested then strength and dose of each should be distinctly written to avoid any confusion.

Directions to the pharmacist or dispenser

The pharmacist or the dispenser should be given clear instructions regarding the prescribed drugs that is pertinent to him. This information usually consists of the amount of the drugs to be dispensed and provision to the patient of any specific drug applying or administering aid. While the later helps the patient use a drug appropriately, the former instructions are meant to ensure that the patient is provided with an amount of drug that is deemed to be therapeutically required by the patient.

Directions to the patient

A standard prescription order contains clear directions regarding the use of the suggested medication. The directions to the patient contain instructions to the amount of drug to be taken, the time and frequency of the dose, and other factors such as dilution and route of administration. If a device is involved in the administration of the medication, the physician and/or pharmacist should educate the patient accordingly and if possible demonstrate how to use. If the drug is to be taken externally only, or to be shaken well before using, or if it is a poison, such facts are also included in these directions.

Because these directions are aimed at the patient, use of abbreviations serve no useful purpose. They should be written in a language which can be read and

understood by the patient or one of his family members. Giving directions in English will not serve any useful purpose in countries where it is not understood by most of the people. Instead, use of some native language should be preferred. The directions should be clear and expressions like "take as directed" or "take as necessary" are never satisfactory and should be avoided. Similarly, directions like "take 8 hourly" are confusing for many patients; a better way is to specify the exact times of the day when the dose is to be taken. Directions regarding the route of administration should also be clearly and legibly written to avoid any inappropriate administration.

Warnings and precautions

A standard prescription order also includes important warnings and precautions pertaining to the prescribed drugs. In many instances these are to be reproduced on the bottle or container in which the drug is dispensed by the pharmacist.

Refill instructions

Regulations regarding the dispensing of drugs exist in most countries of the world. Under these regulations, whereas some drugs can be purchased from over-the-counter, others cannot be dispensed without a written prescription order from the physician. In countries where these regulations are strictly enforced and monitored, the prescribing physician, in addition to specifying the amount that is to be dispensed on each occasion, has to specify the total number of times or the total duration for which the prescription can be refilled. In these countries a patient cannot purchase a drug dispensing of which is prohibited without a prescription order, and cannot repurchase such a drug by showing some old prescription unless refills have been specified by the prescriber. This regulatory measure helps control inappropriate self-medication by the people and misuse of drugs with potential of dependence.

Signatures of the physician

Prescription order is only valid if it has been signed by the prescriber. Signatures are to be made at the end of the prescription in the right lower end. If the name, professional degree, address, and the licence number of the physician are not printed on the prescribing pad, they have to be written in addition to the signatures.

Physicians in the developing countries generally do not follow the standard way of prescription writing

As in the developed countries, doctors in the developing countries learn about the format of a prescription in their medical college years. The basic format taught to them generally resembles the one that has been discussed above. But due to multitude of reasons many doctors in the developing countries do not follow any standard way of prescription writing and it is unusual to come across a prescription that meets the "minimal" requirements of a standard prescription. It appears that

many doctors in these countries view prescription merely as a piece of paper on which drugs to be taken by a patient are written. That is why it is not uncommon to see prescriptions that even do not have basic elements like date, prescriber's and/or patient's identity, and strength of the suggested treatment. Similarly, dosage of the medication is frequently suggested in Latin abbreviations instead of simple native language and related warnings and precautions are mentioned very rarely.

A prescription order is a reflection of the doctor's concern for the patient and significance of a comprehensively written prescription cannot be overemphasized. The minimum that doctors should ensure in this regard is that their prescriptions should be written in a manner that is distinct and better than that of a quack!

Two common "real bad" ways of prescription writing

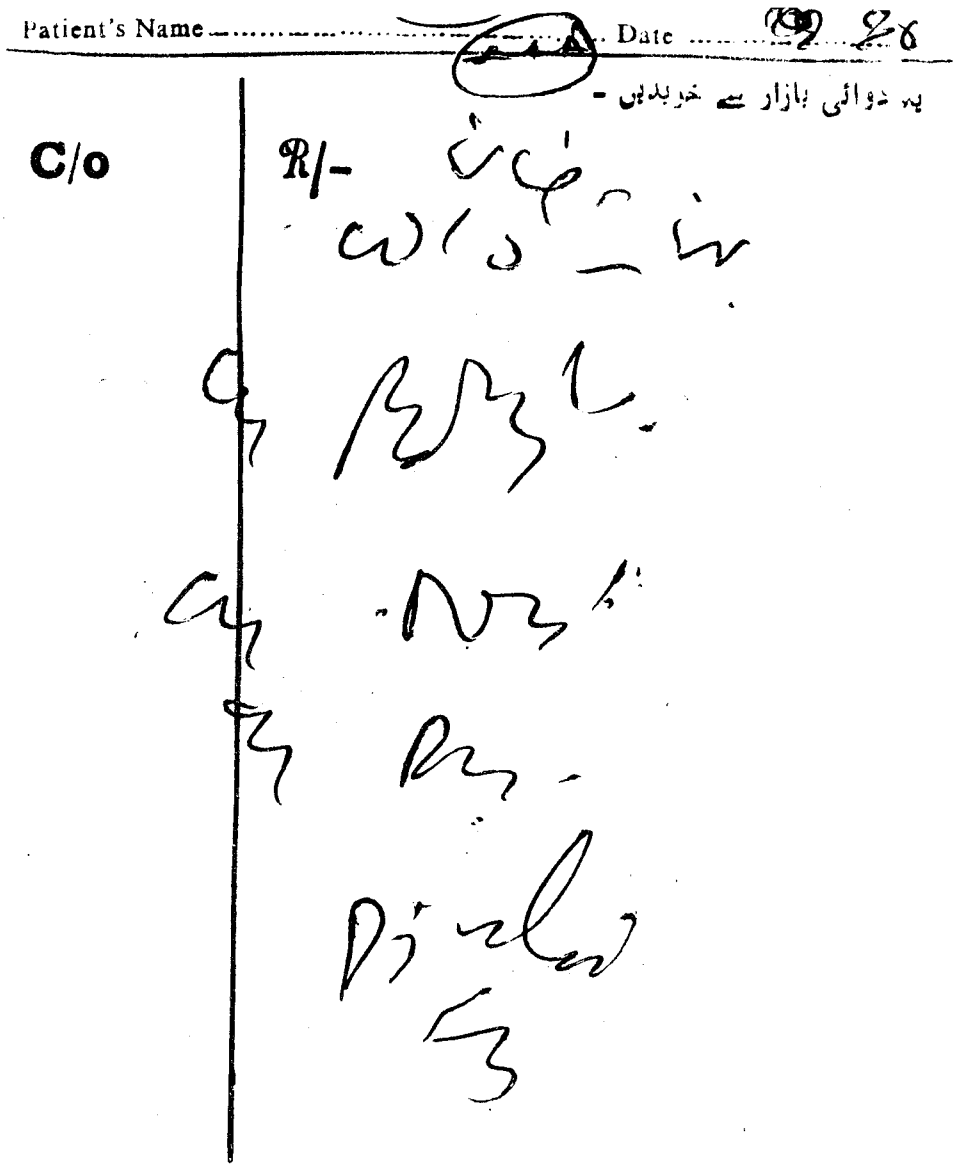
As discussed above, many doctors in the developing countries do not observe the format of a standard prescription while writing a prescription order. Most of such prescriptions are technically inadequate and some of them can be called "real bad" prescriptions. Two commonly observed bad patterns of prescription writing are: (1) prescriptions that are illegible and (2) prescriptions that are written in code words.

Prescriptions that are not legible

Doctors are generally recognized for having a bad handwriting. It is amazing to find someone being proud of an ugliness of one of his characteristics but, not infrequently, doctors do show a pride in their illegible handwriting. When doctors with a tendency to write a prescription in a careless manner scribble it down, prescriptions of the doctors who already have a bad handwriting becomes really hard to understand (Prescription 1).

A prescription that is illegible can lead to numerous errors in the dispensing and use of the prescribed drugs[4]. The dispenser may dispense a wrong drug if he is unable to understand the prescription or he may dispense the right drug in a wrong strength. Similarly, he may misread the dosage and so guide the patient inappropriately. For an illegible prescription the patient will be unable to read any suggested precautions and/or advice and so will be unable to comply to it/them. These errors will not only lead to poor therapeutic results on many occasions, they can also, every once in a while, result in death of or permanent injury to the patient. In countries with poor checks on health professionals a doctor may even be unaware of the disastrous consequences of his negligence. But in countries with an effective system of accountability of the professionals, any such error can be of dire legal consequences to the prescriber (Box 1).

To ensure that the treatment and advice suggested on a prescription is properly followed, and that it does not lead to any harm to the patient, physicians should try to write a prescription order as clearly as possible. If any of the drugs they have



PRESCRIPTION 1. The prescriber has suggested that these medicines are to be bought from a medical store! No wonder if the patient was given a wrong medicine.

Box 1. Prescription should be clearly written

Sir - The serious consequences of negligently writing medical prescriptions have been reemphasized by the court of appeal in the recent case of Prendergast versus Sam and Dee limited and others. Dr Stuart Miller had written a prescription for Mr Prendergast, who was asthmatic with a chest infection, prescribing three Ventolin inhalers (Salbutamol, Allen, Hanburys), 250 Phyllocontin tablets (Aminophyllin, Napp) and Amoxil tablets (Amoxycillin, Bencard).

Mr Prendergast took the prescription to the pharmacy of Sam and Dee limited, where it was dispensed by a pharmacist, Mr Peter Kozary. Mr Kozary dispensed the Phyllocontin and the inhalers correctly, but instead of Amoxil he dispensed Daonil (Glibenclamide, Hoechst), a drug used for diabetes to reduce the sugar content in the body. Mr Prendergast was not a diabetic and as a result of taking a large dosage of Daonil suffered permanent brain damage.

In the high court, Mr Justice Auld indicated that a doctor owed a duty of care to a patient to write a prescription clearly and with sufficient legibility to allow for possible mistakes by a busy pharmacist who might be distracted. Having established that in his opinion the word Amoxil on the prescription could have been read as Daonil, Dr Miller had been in breach of his duties to right clearly and had been negligent. Such liability could not be excused by the argument that their had been sufficient information on the prescription to put Mr Kozary on his guard. Dr Miller's negligence had contributed to the negligence of Mr Kozary, although the greater proportion of the responsibility (75%) lay with Mr Kozary.

On appeal, counsel for Dr Miller argued that the word on the prescription standing on its own could reasonably have been read incorrectly. However, various other aspects of the prescription should have alerted Mr Kozary to the fact that something was wrong. The strength prescribed was appropriate for Amoxil but not for Daonil; the prescription was for Amoxil to be taken three times a day while Daonil was usually taken once a day; the prescription was for only seven days' treatment which was unlikely for Daonil, Ventolin and Phyllocontin were well known treatments for asthma and it would have been unusual to have diabetes and asthma treatments on one prescription and finally, all prescriptions of drugs for diabetes were free under the National Health Service but Mr Prendergast did not claim free treatment for the drug. All of these factors should have raised doubt in the mind of Mr Kozary and as a result he should have contacted Dr Miller. Therefore, the chain of causation from Dr miller's bad handwriting to the eventual injury was broken.

Lord Justice Dillon rejected this argument in the court of appeal. First, it was no defense to Dr Miller to rely on the already established negligence of Mr Kozary when he himself had been in breach of his own duty of care to right clearly and had been negligent, Secondly, those other factors were not enough to make it beyond reasonable foreseeability that Daonil would be prescribed. Therefore, the chain of causation had not been broken.

The implications of his decision are that doctors are under a legal duty of care to write clearly, that is with sufficient legibility to allow for mistakes by others. when illegible handwriting results in a breach of that duty causing personal injury, then the courts will be prepared to punish the careless by awarding sufficient damages. Liability does not end when the prescription leaves the doctor's surgery, even if the doctor has been grossly negligent. It may also extend into and be a cause of the negligence of others.

Source: Mullan K. J R Coll Gen Pract. 1989, 347-348.

prescribed is not in common use they should preferably write it in capitals. The strength of every drug should be specified and for drugs with strengths less than one, a zero should precede the decimal to avoid it being overlooked. Abbreviations, whether used for the drug, its strength, its dose and frequency, or while giving advice and precautions to the patient, can cause confusion and should always be avoided.

Prescriptions that are written in code words

It is not unusual to come across prescriptions that are written in code words (Prescriptions 2). Such prescription orders are usually written by doctors who, in addition to seeing patients, dispense medication to them as well. The dispenser in such clinics is "qualified" to decode the prescription and dispense drugs as ordered by the doctor.

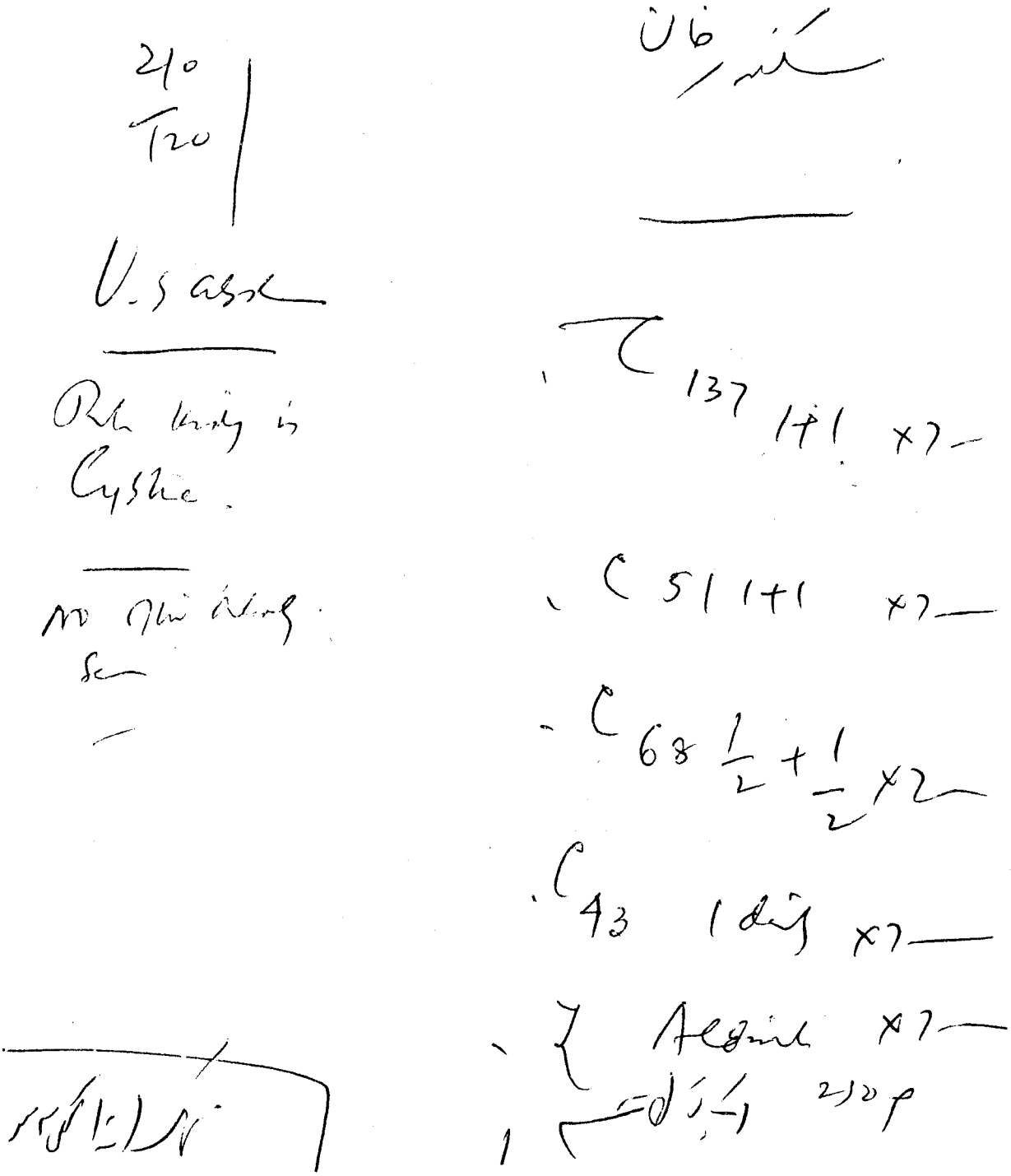
The underlying motive of prescribing in code words usually is to "earn more" and "not to loose the patient". Because of the code words the patient or anyone else is unable to know exactly what has been prescribed. The doctor then can charge from the patient according to his discretion. Similarly, if the patient feels improvement with the dispensed treatment and wants to get some more, he will have to re-consult the same doctor who may charge him with some more fee. Even if the patient does not feel any better and just consults the doctor to ask him what exactly he was prescribed, the doctor can persuade him for another therapeutic trial!

Use of code words in a prescription order does not have any justification. It is just a form of quackery and malpractice. To be ethical and rational practitioners, doctors should never try to conceal the treatment they have suggested unless it is meant to serve some real benefit to the patient.

Standard way of prescription writing is not comprehensive enough for use in the developing countries

The format of a standard prescription as discussed above is the one employed by the developing countries and as such it is not comprehensive enough to meet the requirements of the developing countries (this however does not imply that physicians are justified in just scribbling down the treatment they want to suggest without following any format). The major reason for this is the lack a proper system of medical record-keeping in these countries.

Generally there is no formal system of medical record-keeping in the developing countries and patients have to maintain their medical records on their own. Considering the high illiteracy rates of these countries, it is not surprising that many patients just do not bother to maintain any such record and most of those who want to maintain it are unable to do so. Record keeping further become difficult when the amount of the papers they are handed over in a therapeutic encounter, specially when they consult someone in a teaching hospital, is taken into account. These



PRESCRIPTION 2. A good way to conceal the suggested treatment. But is this a professionally justifiable practice?

papers, in addition to a hospital card or a prescription order, may include: prescription slips for drugs to be taken from the hospital dispensary, prescription slips for the drugs to be bought from a medical store, investigation orders and their duplicate copies, receipts of the various payments they have made, and the results of the investigations they have been suggested. Patients who are unable to sort these papers out simply make a bundle of all the papers handed over to them in their encounter with the health facilities. This bundle, specially when the papers in it are not in an order, is difficult to go through by a busy doctor who, therefore, will be unable to determine what the patient had been through in the previous visit/s and will simply replan a therapeutic intervention. Many of the patients who attempt to sort these papers out, not infrequently, end up with throwing away the useful ones while retaining the useless. For example, it is not uncommon to see patients retaining the duplicate copies of the investigation request forms or the receipts of their payments while not having the previous prescriptions and test results with them. Again because these patients do not have the record of the previous therapeutic interventions a doctor is unable to precisely determine the past medical history of the patient and has to proceed afresh.

The problem of poor medical record keeping in these countries is compounded by the fact that most of these countries also lack any organized system of patient referral. Patients can consult any doctor in any hospital or a private setting provided they have the means to make the consultation. Similarly, they can switch over from one doctor to another on their own without any formal referral. Even if a patient consulting someone in a government hospital wants to continue treatment from the same doctor he might not be able to do so due to different reasons: the doctor might have been transferred from that hospital or that department, he may be in the same department but performing duties somewhere else, or simply he may be on leave.

When a doctor is consulted by a patient who had been previously under care of another doctor, he is in need of the patient's medical record to determine what the patient had suffered from, what investigations he had been through at that time, what were the results of those investigations, and what treatment he had been receiving, to plan an appropriate therapeutic intervention. In view of the fact that many patients may not have any medical record with them, the doctor is likely to repeat clinical procedures unnecessarily and prescribe drugs that have not benefited the patient in the past or that had caused significant adverse effects.

In the situation of inability to maintain their medical records, patients generally are likely to retain a prescription order because it is of significance to them - it is the paper they had been showing to the medical-store keeper to buy drugs. In the developing countries, the prescription therefore should not only serve the purpose of a prescription order, it should also be the document on which patient's brief medical record has been documented.

Suggestions for the pattern of a prescription in the developing countries

In view of the facts that most of the patients in developing countries are unable to maintain their medical record and that no formal system of patient referral exists in these countries, a "prescription" should be something more than a standard prescription order employed by the developing countries. It preferably should include a brief background of the patient and his illness, and a summary of the therapeutic interventions (investigations, treatment etc.) he has received. (If someone is uncomfortable with calling it a prescription he can call it a "medical history and prescription"). Such a "prescription" can serve a more useful purpose than a standard prescription order in the developing countries and suggestions for its format are described below (Prescription 3).

1. The prescription order should always identify the prescriber. Using a printed form containing the name and address of the prescriber is a good practice. Preferably such a form should also have the prescriber's licence number on it. By specifying his licence number on the prescription a doctor can convey to anyone else seeing the prescription that it has been written by a qualified and registered doctor. Further, if this practice of providing the licence number on a prescription is adopted by doctors in general, it can help patients to differentiate between a quack and a doctor.

2. A prescription order should also identify the patient, at least by his name and address. To help provide anyone else seeing the prescription (e.g., another doctor who is consulted by the patient later on) with the background of the patient it is sensible to write down the patient's education, profession, and marital status on the prescription as well.

3. A prescription in the developing countries must include the presenting complaints of the patient in brief and any significant past or family medical history. This will provide any doctor subsequently seeing the patient with the background of patient's past medical history. It will also help him understand the rationale of the treatment suggested at that time (see below).

4. Inclusion of positive clinical findings on the prescription can help another doctor seeing the patient subsequently to gather more information about the patient's medical condition at that time. It can also help him understand why certain investigations were suggested to the patient.

5 The results of the suggested investigations, specially those of clinical significance, should also be written on the prescription. Because of the inability of most patients to maintain their medical record they, not infrequently, misplace the results of the investigations that had been done in the past. By writing a summary of the results on a prescription they are more likely to get secured and save the patient from unnecessary investigations in future.

Clinical Record

Cough – 1½ years

X-ray chest:
Ch.. inflammatory changes more on Rt side. left side.

Pulmonary Koch's

Had taken ATT for 1 year but irregularly

℞

1) Tab. Lederif 600mg (10

2) Tab Myambutol – INH (30

3) Tab Pyrazinamide 500mg

4) Syp Mydrallin 2

5) Tab Nenlin SA (20

PRESCRIPTION 3. Just a few comments about the past history and radiological findings make the prescriber's rationale of prescribing the treatment obvious. Mention of the patient's poor compliance with the treatment in the past will save any other physician who happens to see the patient from wondering why the patient is using anti-tuberculous treatment for such a long time. It also urges that any physician whom the patient consults should be more scrupulous about patient's compliance to the suggested treatment.

6. Ideally a prescription should contain the diagnosis on it so that anyone else seeing the prescription can determine why the treatment was suggested.

   The diagnosis is not written on many occasions because it has not be reached with certainty. This is specially true for general practice setups where up to 50% of the illnesses may not admit to a precise diagnosis[5]. Many of such patients are in fact managed by the practitioner symptomatically. If the practitioner is unable to write a diagnosis for these patients, it becomes difficult for any other doctor seeing the prescription to determine the rationality of the prescribed treatment on many occasions. For example, it is very difficult to determine the doctors therapeutic aim when seeing prescriptions on which analgesics, vitamins, "brain tonics", and antacids have been prescribed concomitantly. Furtermore, in some situations an attempt by the practitioner to label such a patient with a diagnosis may result in inconsistency between the diagnosis made and the treatment suggested, and consequently will be a source of confusion for any one else seeing the prescription. For example, it is not unusual to come across patients being diagnosed as "depressed" but receiving anxiolytics only; patients being "diagnosed" as having UTI receiving anti-malarials as well; and patients "diagnosed as having amoebiasis receiving antibiotics in addition to metronidazole.

   In instances where a doctor is unable to reach a diagnosis with certainty, or where his suggested treatment is not in accordance with the diagnosis made, writing a couple of lines about the patients symptoms on the prescription can help any other doctor whom the patient consults (or has to consult) later on to understand the rationale of the doctor who had suggested the treatment.

   Writing the diagnosis or "the rationale of the suggested treatment" on a prescription can serve a very important mean of self-check for doctors as well. A doctor's practice of writing the rationale of suggesting a particular treatment can make him more thoughtful for suggesting the treatment because he will then avoid suggesting any medicine for which he himself cannot justify any rationale.

7. Obviously the prescription should contain the name and strength of the suggested treatment.

8. Clear instructions about the dose, side effects of the treatment necessary precautions and any other information pertinent to the treatment should be written clearly in a language that is understood by the patient or one of his family members. Provision of this information to the patient helps improve his compliance with the suggested treatment and is a measure to save him from unnecessary risks of the treatment.

9. Finally, the same prescription should serve as a progress sheet of the patient. Results of the requested investigations, response to the suggested treatment (both desired and undesired), and progress in the clinical condition should be

written on the same prescription in the subsequent follow-ups. If there is no space on the prescription to document the progress a reasonable practice would be to securely attach a "continuation sheet" along with the previous prescription.

All this is not that time consuming

Some (might be many!) doctors might argue against the format of a prescription suggested above with a plea that it is a time consuming exercise to write a prescription in such a detail and doctors generally do not have much time. The fact is that it is not all that time consuming as much it seems to be because:

1. All the information that has been suggested to be written on a prescription is routinely gathered by any good practitioner in his encounter with a patient, even when the patient consults him as an out-door patient. The doctor only has to document the summary of the relevant information on the prescription which on most instances would just require a couple of minutes.

2. Documentation of this information by one doctor will spontaneously provide another doctor, whom the patient happens to see subsequently, with the relevant information. This will not only save his time but also ensure a better management of the patient on many occasions.

3. Finally, even if such a prescription is going to take a bit more time of a physician than if he just scribbles down the suggested treatment, it is going to offer clear therapeutic benefits to the patient. It will also, to some extent, ensure that the doctor evaluates the patient properly and suggests a treatment with a justifiable rationale.

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Chapter 6

Informing The Patient And Monitoring The Treatment

For effective therapeutic care of a patient, a doctor's job does not end with handing a prescription order over to the patient. Doctor also has to make sure that the patient has been reasonably informed, in a language and manner that can be understood by him, about the nature and prognosis of his illness, the details of the suggested treatment, and about the non-medicinal interventions and precautions he has to observe to achieve maximum therapeutic results with minium side effects. Moreover, to achieve the desired therapeutic objective the doctor has to make all possible attempts to ensure patient's compliance with all the suggestions and advice given to him, and to see the results of the suggested treatment and to change or terminate it accordingly the physician also has to monitor the treatment. Physicians' casual attitude in these post-prescription-writing aspects of therapeutics can lead to unsatisfactory therapeutic results, inappropriate use of medication by patients, their unnecessary exposure to side effects of drugs, and waste of their financial resources.

Providing Information To Patients

All patients desire to be provided with information about their illness, the suggested treatment, and the expected therapeutic outcome. In this there is no difference between poorly educated lower-class patients and better educated, upper class patients. However, as uneducated patients are likely to ask fewer questions than the educated ones, doctors may erroneously assume that the former have little desire for such information. In addition to patient attitudes and sociodemographic variables, other factors that have been found to result in individual differences among patients in their information-seeking behaviour are: type of illness, length of doctor-patient interaction, presence of a companion, first versus repeat visit, and the particular doctor seen[1].

In spite of patients' desire for information, it is an observation that patients are generally given little or no information, even on such basic issues as the type of drug used, how it could help the patient, possible adverse effects, and precautions to be observed. In the developing countries doctors often defend themselves for such non-communication on the basis that the patient is illiterate. This overlooks the fact that they fail to give information even to literate patients, and that even illiterate patients are quite capable of comprehending basic facts if presented in simple language[2].

Effective communication between physicians and patients is crucial for the delivery of quality health care[3]. It helps to develop a good therapeutic relationship and achieve good therapeutic results. Informing patients about their illnesses and the therapeutic intervention being made is a one of the factors recognised to contribute to the satisfaction of patients[4].

Patients also need to be informed because the conventional paternalistic model is being replaced by the concept of shared decision-making[5]. With growing awareness and options of treatment forms and facilities available, patients in the developing countries also tend to look into the help offered to them critically, desire to learn about their illness and the treatment they are offered, and participate in decision making. In this approach both doctors and patients make active and essential contribution in decision making. This new model of health care demands that patients should be comprehensively informed about their medical condition and the therapeutic alternatives so that they can fully participate in the process of decision making.

Clarity and completeness of communication between the patient and the doctor and the "outcome" of the encounter has been recognised to be one of the factors contributing to patient's satisfaction. Physicians often believe that they do an adequate job of communicating with their patients, but what physicians think they are communicating and what patients actually understand do not always coincide[6]. Physicians, therefore, should not only provide their patients with all the information relevant to the clinical situation under consideration, they should also ensure that the patients correctly understand what they have been told.

Informing about the nature of the disease, its prognosis and the therapeutic objective

Illness is a causes of physical, psychological, and social distress. Understandably, anyone who is sick desires to know about the illness that is causing all this distress. Whether he expresses it in front of his doctor or not, he is also keen to know what is going to be done to relieve him of the suffering - his illness, and to what extent he will be cured. Physicians need to appreciate this very obvious human desire of their patients and inform them accordingly, right at the outset of the therapeutic encounter.

Informing patients about the nature of the disease, its prognosis, and the therapeutic objective facilitates the therapeutic relationship. It helps a patient to understand what is "wrong" with his body and what is the physician going to do to "correct" it. Not conveying to a patient these essential facts of his illness, and the desired therapeutic aim may leaves him with his erroneous beliefs about the illness and be a reason for therapeutic failure (Box 1).

Patients may be interested in knowing the diagnosis, but more often than not this means very little to them. They are more interested in knowing the details of their

Box 1. Consequences of not informing a patient about the nature of illness and the desired therapeutic objective.

Diarrhoea in children is a commonly encountered problem in the developing countries. In most cases it has a viral aetiology and does not require treatment with antibiotics. It is a self-limiting condition and use of drugs that stop diarrhoea, by one mechanism or the other, are contraindicated due to clearly established medical reasons. The only therapeutic intervention in these cases is to replenish the fluid and electrolyte loss, which if not done effectively can result in fatal consequences. The World Health Organization and similar others are actively engaged in communicating these facts about diarrhoea in children, both to the health workers and the public, for last two decades. But the situation is still far from satisfactory. An important reason for this seems to lie in the fact that physicians do not communicate effectively with the parents of the diseased child about the nature of the illness and the therapeutic interventions being made.

When parents bring a child to a physician for treatment of his diarrhoea, their focus of concern is the child's diarrhoea. They believe that because of it the child is not retaining any of the food he is being given, is being "starved", and consequently going weak. They, therefore, feel that if the child's diarrhoea is stopped the disease will be over. An additional concern for the mother about the chid's loose motions might be that it offers her a lot more washing to do!

Let us assume that the physician these parents have consulted is a one who knows that it is not rational to prescribe antidiarrhoeals and antibiotics in such cases. He knows that the child only needs Oral Replacement Therapy and so suggests on of the preparations. He is very meticulous in telling the parents how to prepare the solution, how to store it, and how frequently to administer it. But he overlooks to tell the parents about the nature of the illness and what is going to be achieved with the therapy.

The worried parents go home and start the suggested treatment believing that it is going to relieve the child of diarrhoea. They administer it as has been directed by the physician but even after a full day of trial they do not find any benefit - the frequency of child's motions is the same. Disappointed with the results they consult another doctor who, to relieve the parents' anxiety and "impress" them with his therapeutic talent, prescribes an antidiarrhoeal. Parents start the new treatment and the diarrhoea is controlled, luckily without any complications to the prescribed drug. Parents not only are happy to see their child recovered but are also convinced of the clinical "competence" of the later physician.

It is quite likely that this situation would not have resulted if the physician who had suggested Oral Replacement Therapy had communicated to the parents the nature of the illness and the therapeutic objective that was desired to be achieved with the therapy. Communicating to the parents in understandable terms that the diarrhoea is a self-limiting condition and any attempt to stop it before its natural course can result in a harm to the child would have eased the anxiety of the parents. Furthermore by telling them that the suggested therapy meant to replace the fluid and electrolyte loss and had nothing to do with stopping the diarrhoea would have ensured that they do not erroneously conclude it to be an ineffective remedy. The likely outcome then would have been that they might have continued with this rational treatment.

illness. When a physician informs a patient about his illness it is important for him to be lucid and explain the things in a way that can be understood by the patient. However, while attempting to be simple in his expression, physician should ensure that he remains as much scientific as possible and does not talk in layman terms or bases his explanation on erroneous cultural concepts. Such an explanation can do more harm than good in long-term.

Patients are very much concerned about the prognosis of their problem because it is the prognosis that determines their future. The doctor should try to be as far sighted and realistic as possible in informing patients about the prognosis. It is valueless to give at the outset a good prognosis in order to spare the patients' feelings, when the true implications of the disease will become apparent in short time. To do so will undermine the patient's confidence in his doctor. On the other hand if prognosis is uncertain, it is indefensible to warn the patient of the worst possible outcome simply to safeguard oneself from future criticism. It should be remembered that the prognosis of an illness also depends upon the patient, that is, the way he follows the suggested regimen, and this should be communicated to the patient.

Similarly, confidence transmitted to the patient about a therapeutic regimen must be based on a realistic view of the disease, the drug, and the probable course of events. Too dogmatic an attitude on the part of the physician can produce disappointments and resultant noncompliance with the therapeutic regimen. Too tentative an attitude on the part of the physician can lead to a sense of "we're all in the dark"[7].

Because patients relate the severity of an illness with the associated distress, informing patients who are suffering from some problem that does not cause much distress, or have obvious physical symptoms is specially tricky and difficult. For example, it is very difficult to convey to patients of hypertension or diabetes mellitus the consequences of their illness if they do not get properly treated and comply to the suggested treatment. This is again something very much human. We all do not appreciate the unfavourable consequences of our unhealthy habits unless the consequences get manifested! Showing resentment toward such patients for their noncompliance to the suggested treatment is not going to do much good. These patients require a through explanation of their illness which needs to be done with patience.

Informing about the details of the suggested medication

There is considerable evidence that patients want to know more about the drugs they take[6]. They want to know what the drug is, how it is going to cure their illness, is it going to harm them in anyway, and how and for how much duration it has to be taken. Furthermore, any medicine, however good, that is not accompanied by adequate written or spoken information is liable to become a "problem" drug in the patient's hands[8]. Therefore, when a doctor prescribes for a patient it is incumbent on him to communicate to the patient the frequency of administration, the duration of treatment and possible side effects.

Informing about the dose and frequency

Patients take the medicine that has been suggested to them, physicians only prescribed it. If a physician does not inform the patient about the dose and frequency of the suggested medication the patient is likely not to take it properly. A poor communication by the physician in this regard can leave the patient confused and result in poor compliance to treatment by him. To ensure that patient understands clearly, the physician should explain in a simple language. To save the patient from any confusion after he has left the clinic, physician should write the dose and frequency of the suggested regimen clearly in a language that is understood by the patient or one of his family members, on the prescription. To be further scrupulous in this regard a physician (specially general practitioners) can keep a liaison with the nearby medical-store keeper, from whom most of his prescriptions are purchased. He can be requested that while he sells out the requested medication, he should explain to patients the dose and frequency of the suggested treatment, as is written on the prescription order, and if possible write it on the packing of the drug as well.

Informing about the duration of treatment

It is not uncommon to see patients asking, "Doctor, how long will I have to take this medicine?" While most of them ask this question because they relate termination of the treatment with complete cure of the illness, others might be interested in knowing the duration of treatment to assess the likely cost. Patients are also likely to relate the duration of the treatment with the severity of illness - the longer the duration of treatment the more severe the illness. An openness with patients about the expected duration of treatment, particularly for medications for which duration of therapy is not clear, is important in establishing credibility and giving the patient reasonable expectations of drug therapy.

When informing a patient about the expected duration of treatment, it is also important for physicians to tell their patients when to expect the therapeutic results. Some conditions, for example, fungal infections of skin, gastric and duodenal ulcers, tuberculosis, and depression improve slowly after the initiation of treatment. If a physician does not inform a patient accordingly, the patient, when not seeing much of therapeutic response, is likely to discontinue the treatment with a view that it is ineffective. Similarly, for conditions like epilepsy, hypertension, and diabetes mellitus, it is also essential to inform the patients that the treatment will have to be continued for certain period of time or life-long, even when there are no obvious complaints are symptoms. Inability of a physician to do so may result in patients' discontinuation of the treatment as soon as he thinks he has "recovered".

Informing about the side effects, warning the patient and suggesting precautions

All drugs have side effects. These are the effects that are not desired for therapeutic purposes but cannot be avoided. Side effects of most drugs are predictable but which specific side effect appears in an individual patient, or toward which of them he

specifically shows intolerance, vary from one patient to another. Patients should be informed about the side effects of the drugs they have been suggested due to two important reasons:

1. It is the ethical (and legal) right of the patients to be informed about the adverse effects and risks inherent in any treatment. We all are well aware of this; that is why we get consent of patients (or one of their family members) to proceed with interventions and procedures carrying a potential risk to the patient. (Though such a consent form reads something like "I have been fully informed about the risks of the procedure and am willing to undergo it", how far patients in the developing countries are really informed cannot be commented upon!). To be an ethical and rational practitioner, physicians should communicate to their patients the adverse effects inherent in any treatment.

2. Many drugs produce side effects that give a bad feeling or sense to the patient. The bad taste given by metronidazole, dizziness caused by many antiepileptics, antidepressants and conventional antihypertensives, gastrointestinal upset caused by many antibiotics and NSAIDs, anticholinergic effects given by many psychotropics, and "mental dullness" caused by conventional antiallergic drugs are some such examples. Because of the "bad feeling" associated with the use of these drugs, a patient is likely to discontinue the treatment as soon as he feels somewhat improved, if he has not been informed and reassured about these side effects.

To protect patients from any harm that may result from the suggested treatment, they have to be warned against specific undesired effects of the suggested medication. Further, they also have to be told about the precautions they should observe when taking any particular medication. If a patient is not informed about the side effects that are to be reported to the physician when they appear, he is likely not to pay attention to them if they appear. This may result in harm to the patient that may be irreversible in some instances. For example, the consequences of not telling a patient who is started with valproic acid or carbamazepine therapy to report back immediately if he develops sore throat, not informing the patient who is put on some antidiabetic treatment about the symptoms of hypoglycaemia and how to respond to them, or not telling a patient who has been suggested treatment with some sulphonamide to consult the doctor immediately if he develops a rash, are very obvious. Similarly, to protect patients from a possible harm or to achieve optimum therapeutic results they have to be informed about the precautions they have to take, either because of their illness or the suggested treatment.

Giving advice regarding non-medicinal interventions

As discussed in chapter 3, rational therapeutics does not only involve prescribing drugs to a patient. To be rational, and to achieve maximum therapeutic results, doctors also need to focus on the non-medicinal interventions that can be of benefit in any particular therapeutic situation. Not properly and clearly informing a patient

about any such interventions may result in poor therapeutic outcome or unnecessary suffering to a patient.

In providing any non-medicinal advice to a patient it is important for a doctor to try to visualize the patient's real problems and understand him in his context. Providing a stereotyped advise to all the patients of the same illness may not be enough. Any such advice needs to be specifically "tailored" for different patients due to individual differences among them. For example, every undernourished patient cannot be told to take an egg, a glass of milk, and a minimum of x grams of meat a day; the patient might have erroneous ideas about the effects of taking an egg a day, he might have a distaste for meat, he might have a belief that milk is "bad" for his gut, or simply he might not be able to afford such a diet.

Significance of letting the patient express his ideas

Patients should also be provided an opportunity to express their views about their illness and the suggested treatment. This helps the physician to have an idea about the patient's perceptions about his illness and the suggested treatment and is satisfying for the patient as well. In a study, patients who felt they were educated about their medical problems, had an opportunity to express their ideas about the nature and treatment of these problems, and discuss areas of life stress with their physician, were more satisfied than patients who felt they had not received any or all of these types of interventions[9]

A physician must welcome patient's response regarding the effectiveness of the suggested treatment or its failure. He should not show resentment towards the patient if the response to the suggested treatment is poor or if the patient is "bothering" him for the uncomfortable effects of the drug/s. Instead, the patient should be listened to for whatever he is experiencing with a drug. Though side effects of the commonly used drugs are well established, there are individual variations in the way different people experience them and react to them. Not effectively communicating to the patient that you understand what he is experiencing, and not making an effort to reassure him, or if needed to change the treatment, will lead to loss of patient's faith in the treatment, and change of the doctor on many occasions.

Specially tricky is the situation when a patient is improving with the suggested treatment clinically but is not satisfied with the progress, or contrarily, when he thinks he has significantly improved while in fact he has not. The former situation is frequently seen in conditions that have prominent somatic symptoms and respond slowly to treatment. The later is seen for conditions that have few evident symptoms on the basis of which patient can monitor the progress. In both these situations physician should attempt to "understand" the patient and inform him accordingly.

Consequences of not informing the patient about the details of the treatment

Consequences of not informing the patient about the details of the treatment can be elucidated from the above discussion. To summarize, they are:

1. Patient might not be clear about the dose and frequency of the suggested treatment and, thus, will use it inappropriately. The uncertainties of patients about the prescribed regimens contribute to the failure of many of them to benefit fully from their medications. Evidence suggests that inadequate communication about drugs is one of the principal reasons why 30-55 percent of patients deviate from their medical regimens[6].
2. Patient might discontinue the treatment due to intolerance to the side effects for which he was not informed and reassured.
3. Patients might make efforts to get the relevant information from other sources, that might be wrong and of not much help to them on many instances. The uneducated might ask the dispenser or from whom he has purchased the medicine or some other "knowledgeable" or "experienced" person. The educated one may resort to getting the information by reading the leaflets contained within the packing of the drugs.
4. Patients with diseases not causing obvious physical symptoms might discontinue the treatment believing that they are not sick. While patients with diseases that improve slowly may keep on shifting doctors with a view that the treatment is not offering any benefit.
5. Patient might remain ignorant about the serious side effects that may cause irreversible damage and are to be reported to the doctor as soon as they appear. He may also remain unaware of the precautions he has to take while receiving any particular drug.
6. Patient will not effectively comply to non-medicinal interventions that might be essential to achieve maximum therapeutic benefits.

Monitoring The Treatment

Once a treatment regimen has been advised by a physician it is his professional obligation to monitor it. Treatment has to be monitored to see how much benefit it is offering to a patient and to observe for any undesired effects and, when more than one drug is being used, for probable drug interactions. While monitoring the treatment, physician also has to ensure that the patient is complying to the regimen as has been suggested. Finally, physician has to monitor the treatment so that he can terminate it once the therapeutic objective has been achieved.

Monitoring the treatment for the desired effects

Whenever a physician suggests a therapeutic regimen he should be clear about what he wants to achieve through it. As discussed previously the desired objective should

always be realistic and rational. If the expected desired-effects are not being achieved with a drug it will need to be changed with some other. When changing a treatment regimen, physicians should bear in their minds that patients interpret this change in treatment in different ways. While some will be happy with any such change, others are likely to attribute it to physician's incompetence, specially if they had not been informed about the likelihood of poor therapeutic outcome with the treatment they already were receiving. Any such change in treatment should, therefore, be carefully and clearly explained to the patient.

A patient who is not satisfied with the therapeutic progress, even when the physician is, is likely to discontinue the suggested treatment or switch over to some other doctor. Such patients need frequent reassurance about the progress and the physician should take care of providing it. Similarly, some patients may erroneously assume that they have recovered because they would not be having any obvious symptoms. Such patients will require repeated explanation about the nature of their illness to make them comply with the treatment.

Ensuring patient's compliance with the suggested therapeutic regimen

Drugs are taken by the patient. There is a convenient myth that doctors give treatment. Doctors rarely treat; they usually give advice. The doctor must prepare the patient to accept, remember, and to follow his advice.

A correct diagnosis and appropriate treatment are of little value if the patient does not follow the treatment prescribed. To achieve the desired therapeutic objective a physician should ensure that the patient is complying to whatever regimen he has been suggested. While checking for compliance, physicians should remember that very often patients do not speak the truth when they assert that they have taken their medicines[10]. Similarly, several studies have highlighted the discrepancy between the prescriber's perception of what patients are receiving and their actual drug intake[11]. Physicians, therefore, should be very scrupulous when determining a patient's compliance with the suggested treatment.

Poor compliance to treatment is an important reason for therapeutic failure. Whenever a physician does not see the expected progress in a patient's condition, the first thing he should think of must be "is the patient taking the treatment as he has been suggested?" Any change in a treatment should be only made after patient's compliance to it has been ascertained.

The problem of non-compliance

Non-compliance is now a days considered to be a major problem in the health services of both developed and developing countries. A recent review of the literature suggests that the compliance rate is approximately 50% and decreases with time.

Another analysis shows that between 30% and 75% of patients do not take all the drugs prescribed, do not take them in the prescribed dosage, or use them wrongly; and 40% of the mistakes may be harmful. The low compliance rate with effective remedies results in the failure of curative or preventive treatment and may have negative effects on the patient and society, such as the development of resistant strains, or economic costs[12].

Factors influencing compliance

Like prescribing, compliance is a complex phenomenon. Much research has gone into attempts to define the most important factors influencing compliance; but the results vary and are difficult to systematize. The illness, the treatment, the form in which the drug is administered, and the number of doses or of preparations to be taken daily all have a positive or negative influence on compliance. An association has been established between noncompliance and the number of concurrent medications prescribed. Noncompliance also increases when patients misunderstand instructions for using prescribed medicine[13].

Many investigators have found higher compliance levels when the prescriber provides ample information and follows up the patient attentively. These results, however, have not been confirmed by a recent study based on 185 compliance studies: An interesting finding at sharp variance with conventional wisdom is that there appears to be no relationship between patients' knowledge of their disease or its therapy and their compliance with the associated treatment regimen. That this is so is supported by a lack of association between patient's intelligence or educational achievements and compliance. Non-compliance then becomes a voluntary act of the patient, who evaluates the behaviour of his doctor and the drugs prescribed in the light of his knowledge of and beliefs about the illness and the drugs, which are not always rational and influenced by education[14].

It is significant to note that no association exists between noncompliance and factors such as age, sex, level of education, and duration of disease[13]. The most important factor that seems to influence compliance is the doctor; a study has shown that compliance improves when the doctor demonstrates that he is competent and takes the situation and the needs of his patients into account[14].

Improving drug compliance

Patients' compliance to the suggested regimen can be improved by simple means like keeping the regimen simple, providing clear instructions to the patient, and taking care of patients' beliefs, dislikes, and financial limitations while planning the regimen. (A scheme by which a patient's compliance to the treatment can be improved is given in Box 2.)

1. It is difficult for any patient to remember and follow complicated regimens. Attempt should be made to keep the regimen as simple as possible; an easy way to do this is to prescribe the minimum number of drugs.
2. Miscommunication between a doctor and patient can be a cause of non-compliance. It is difficult for patients to follow a health care regimen that he or she does not understand. To improve their compliance, it should be ensured that patients are provided with clear instructions, both verbal and written, about the suggested regimen, and that the patient has understood whatever he has been told (Box 3).
3. While suggesting a treatment regimen patient-factors should be born in mind. Efforts should be made to prescribe a regimen that is convenient for the patient to carry out, that is within his financial sources, and for which patient does not have particular disliking or repulsion due to his beliefs or previous experiences.
4. When a patient is found to be experiencing benign but uncomfortable side effects, he should be reassured and significance of continuing the treatment should be explained to him.

Box 2. Improving compliance with drugs.

There are several ways to improve compliance. Even with complicated regimens, compliance is possible if the patient is capable of learning.

1. For patients who seem apathetic about their problems, emphasize the importance of taking prescribed doses so that the physician can interpret the results of therapy.
2. Be understanding and forgiving but firm with patients who are capable of good compliance. At the first visit, it may be useful to reach an understanding of the importance of regular drug intake.
3. Ask frequently about drug compliance. Have the patient (or guardian who manages the pills) recite, at each visit, the number of each tablet taken and when each is taken during the day. The patient will come to expect the question and will therefore learn the daily regimen. Since alternate day regimens are usually unnecessary and a good excuse for getting confused, they should not be used.
4. An effective technique for improving compliance, and one that the physician should insist on in difficult cases, is the "morning set-up plan. Insist that the patient (or the guardian) count out the entire day's dose of medications on awakening in the morning; place the tablets in the designated place such as a cup or a separate pillbox. Draw from this receptacle as needed for the day's dose and inspect it at bed time to be sure the day's dose is entirely consumed. Repeat the procedure each day. Well-educated patients will resist such an elementary procedure; ignore these complaints and insist that it be followed.

"Adapted from: Porter RJ. General principles: How to use antiepileptic drugs. In: Levy RH, Dreifuss FE. Antiepileptic drugs. New York: Raven Press Ltd. 3rd ed. 1989. p125-126."

5. Patients who are at high risk of noncompliance should be identified and special efforts should be made to improve their compliance. Such patients include, those who are being treated for conditions not causing obvious symptoms or distress, those under psychiatric care, those who are under long-term treatment, those who are socially isolated, and those who have deteriorating cognitive functions.

Box 3. Non-compliant, or illiterate?

SIR, - Dr Frankel's paper (Dec.26, p1515) brings to mind a similar experience. As a resident I was caring for a number of outpatients, one of whom was a black woman in her mid-20s with severe hypertension. Her blood pressure control was poor, necessitating weekly visits. Every week, I adjusted and readjusted the medications we had available in the late 1960s without substantial improvement of her blood pressure. Frustrated, I admitted her so that consultants could see her and consider bilateral nephrectomy, a treatment in vogue at that time for severe hypertension. To my astonishment, when she was on bed rest and on the same anti-hypertensive drug regimen, her blood pressure came under prompt control. drugs were discontinued and good control was maintained even when she became ambulatory about the ward. It was then that I learnt that she could not read the prescription labels. My detailed weekly adjustments could not be implemented. As frankel points out, she was not non-compliant but unable to comply. I was humbled by the experience and horrified that someone of my own age, raised in the United States in the second half of the twentieth century, was quietly carrying this burden of illiteracy. Perhaps it is fortuitous, but Frankel's case and mine were in the same city.

Rossof AH. Non-compliant, or illiterate. Lancet 1988;i:362.

Monitoring the treatment for undesired effects and drug interactions

All drugs have adverse effects which are not only a reason of inconvenience and discomfort to the patient but a cause of morbidity on many occasions as well. As has been commented by the British Committee on Safety of Medicines in 1985:

> *"At the beginning of the twentieth century syphilis was the great mimic of systemic disorders. Later, tuberculosis took over this role. Both of these diseases have been tamed by chemotherapy and now "drugs" head the list of disease simulators*[15]*."*.

When a physician prescribes a drug he should be aware of its potential adverse effects so that he can effectively monitor their appearance. Similarly, when prescribing more than one drug to a patient he should be aware of the possible interactions that can occur and should monitor the patient accordingly. A physicians ignorance about the adverse effects of, or possible interaction between the drugs he has prescribed, either through lack of knowledge or due to lack of adequate observation of the patient, can be of dangerous consequences to the patient.

Sometimes physician approach the appearance of adverse effects of a drug by prescribing some more drugs to "neutralize" these effects. The approach might be justified on some occasions but does not carry much rationale on many instances. A reasonable approach is to make alterations in the dose, frequency, time and mode of administration, or the preparation to get over these effects. For example, if the gastritis associated with short-term use of NSAIDs can be taken care of by advising

the patient to take the medicine only after meals, there is no fun in prescribing antiulcer drugs and antacids to him.

Patients who are severely ill usually receive several drugs, and it may be difficult to distinguish iatrogenic toxicity from the symptoms and signs of underlying disease[16]. A deterioration in the symptoms or signs of a previously stable patient, therefore, should always raise a suspicion of an iatrogenic toxicity. Similarly, patients who are particularly susceptible to drug adverse effects and interactions (TABLE 1) should be monitored for any such effects more vigilantly.

Table 1. Patients particularly susceptible to drug adverse effects and interactions

1. Elderly patients receiving many drugs.
2. Patients who have acute illness; for example, severe anaemia, left ventricular failure, status asthmaticus, pneumonia.
3. Patients dependent on drug treatment; for example, transplant recipient, connective tissue disorder, Addison's disease.
4. Patients who have unstable disease; for example, epilepsy, diabetes mellitus, cardiac arrhythmia, dementia.
5. Patients who have considerable hepatic or renal impairment; for example, cirrhosis, congestive heart failure, uraemia.
6. Patients who have more than one prescribing doctor.

Reproduced from: Brodie MJ, Feely J. Adverse drug interactions. BMJ. 1988;296:845-849.

Terminating the treatment

The withdrawal of drug treatment once the initial indication has resolved often requires greater initiative and discipline than initial prescribing[11]. Stoping an established treatment is difficult for both the doctor and the patient, perhaps because of their fear of a relapse. That is why doctors may not stop the treatment even when the illness has been cured or it has remitted. This is specially true when a patient is being managed for some chronic illnesses like tuberculosis, asthma, connective tissue disorder, epilepsy, or a chronic psychiatric or dermatological disorder. Not infrequently, these patients consult a doctor or get his "attention" only when they start experiencing some of the adverse effects of the treatment that are manifested only after their long-term use.

Physicians should ensure to stop the treatment once the desired therapeutic objective has been achieved. Continuing a treatment beyond the scientifically recommended period merely because of a fear of relapse does not carry any justification and exposes patients to unnecessary risks. Patients, specially those who have recovered after some long-term therapy, should be explained and reassured that stopping the treatment is not going to cause them any harm otherwise they are likely to continue it on their own.

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Section 2

Factors Influencing Therapeutic Judgment And Decision

"Physicians are characteristically rational and responsible, but it is nearly impossible for them to appear so if they respond to the pressure of time, uncritical reading, industrial advertising, and the persuasion of "detail men" and patients to use the flood of new drugs without proper education in therapeutics and without sufficient knowledge about or rational expectations of each drug."

"Smith WM. Drug choice in disease states. In: Melmon KL, Morrelli HF (ed.). Clinical pharmacology - Basic principles in therapeutics. USA; New York, Macmillan Publishing Co., Inc. 1978. p6."

Chapter 7

Medical School Training

Medical school education and training primarily aims at enabling the students to identify (diagnose) and treat diseases. It is after the successful completion of this training and, in some countries, a compulsory one year internship, that the students become doctors and are allowed to practice medicine independently. They get the licence to take care of the sick and prescribe medicines. How effectively, rationally, and ethically they use this licence is, to a great extent, determined by the training they had received. This training also determines their awareness of the pressures and factors that are going to influence their therapeutic judgment and decisions when they are in practice, and the way they respond to them. The role and influence of the medical school education and training on the prescribing pattern of doctors, therefore, is very obvious and cannot be overemphasized.

Current status of medical-school education

Unfortunately modern medical education and training does not deal as effectively as it should with the education of physicians in therapeutics. Numerous deficiencies have been recognised in the current curricula of medical school education by experts in both the developed and the developing countries[1-7] (Box 1). Teaching is mostly didactic and textbook oriented. Pharmacology is taught in a theoretical context. Clinical training is given in a set-up which differs significantly, specially with reference to academic and therapeutic facilities, from the one where most of the graduates are to serve after graduation. Importance of correct diagnosis is emphasized but applied aspects of pharmacology and therapeutics are not paid much attention to. It concentrates too much on accumulating quantity of facts rather than teaching techniques of problem solving and making a rational choice between drug treatment alternatives. Students are not taught how to evaluate critically any new information about drugs. Humanistic and social aspects of medicine are given little attention. Preventive aspects of medicine are also not signified and the fresh graduate fails to recognise that his responsibility is to take care of his patients' health in general and to educate them about basic health principles. Consequences of such a training is that although basic medical knowledge and ability to make a diagnosis is acquired, practical and rational prescribing and patient-managing skills remain weak.

These deficiencies in training, as discussed below, contribute to the global problem of inappropriate and irrational prescribing by the physicians. They also make their therapeutic decisions vulnerable to the adverse social and industrial pressures, that further add to their irrational patterns of prescribing (Figure 1). A need for improving the education of physicians, therefore, has been stressed for by the experts throughout the world:

1. An official UK Committee on Effective Prescribing has advised that doctors are not trained sufficiently in basic drug use and prescribing; and recommended more training for doctors, both before and after they qualify[8].

2. The American College of Physicians recognizes that the "drug revolution" provides physicians with the opportunity to treat patients more safely, rapidly, and effectively than ever. To take full advantage of the potential benefits new developments in drug therapy offer to patients, and simultaneously to control the potential dangers these developments offer, the American College of Physicians recognizes the need for improved education of physicians and other health care professionals in rational therapeutics[5].....

Box 1: An examination of existing curricula in medical schools

An examination of existing curricula in medical schools reveal:

- Lack of communication between health authorities who deliver the service and the medical schools which produce manpower for the delivery of the health care services
- No feedback given to schools regarding skills, knowledge, attitudes and competency the graduates will need to deliver those services.
- Lack of balance between curative and preventive medicine.
- Emphasis on classroom hospital-based education; little exposure to community.
- Exposure of students to ill patients in the hospitals. Many of these patients are at the terminal stages of their diseases.
- The learning situation (hospital) is quite different from the working environment (rural health centers) for majority of doctors in Third World countries
- Predominance of departmental, subject centered curriculum linked with high technology medicine. This gives a heavy burden on medical students to retain knowledge they acquired in their basic science years until it is needed in clinical work.
- Low priority of community health in curriculum; because of this, fundamental sciences like medical sociology, medical anthropology and medical economics, necessary to understand the community, are totally absent.
- Teacher-dependent learning process, resulting in lack of self-reliance and self-confidence in students..
- Communication between teachers and students is strictly one way, via lectures. There is lack of any dialogue between the two and students' experiences are ignored
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Reproduced from: Chowdhury Q. Overview of problems and framework for undergraduate medical/pharmacy curricula. In: Balasubramaniam K (ed.). Towards rational drug use - Proceedings of the international consultation on rational drug use in undergraduate medical/pharmacy education; Manila, Philippines; 13-18 August 1988. International organisation of consumers unions, regional office for Asia and the Pacific, Malaysia 1990. p26-27.

3. According to an expert from Bangladesh, "In order to produce medical graduates who can compassionately respond to the health needs of the communities they serve and to assist the people and the state to achieve their health objectives within the resources available, there should be reforms in the existing curricula. These should include changes in the teaching and learning approaches[7]."

4. According to WHO: "Many developed countries and most developing countries have failed to recognise clinical pharmacology as a service speciality and neglected its potential contribution to undergraduate training. Although the impact on rational drug use will be long-term, improved undergraduate education in clinical pharmacology is likely to be one of the most cost-effective ways of improving prescribing.

Figure 1. Consequences of poor training in applied therapeutics.

Poor training in therapeutics - How age, gender, occupation, socioeconomic status and cultural beliefs of the patient effect the choice of drug; significance of providing information and instructions to patients; significance of compliance with treatment and factors effecting it; importance of non-medicinal interventions and health education of the patient; inability to critically evaluate any new information about therapeutics etc.

Vulnerability to adverse influences:
Patient pressure: Suggesting investigations or prescribing useless and ineffective drugs or drugs not needed in that particular case, just to satisfy the patients' desires and expectations.
Commercial demands: Prescribing drugs or suggesting treatment (e.g., intravenous dextrose-saline infusion) just for the sake of earning some money; parenteral use of drugs to relieve symptoms rapidly for the sake of retaining the patient.
Pharmaceutical industry tactics: Getting misinformed about the utility and effectiveness of certain drugs and consequently:

- prescribing drugs of unproven efficacy, e.g., brain tonics;
- prescribing for conditions that do not require drug therapy, e.g., common cold, diarrhoea in children;
- resorting to drug therapy when non-drug therapy can be equally effective and more safe, e.g., reassurance for mild situational insomnia, exercise and diet control for obesity;
- prescribing drugs of higher cost when cheaper but equally effective are available.

Consequences
Ineffective and expensive treatment; exacerbation or prolongation of illness; unnecessary exposure to side-effects; reinforcement of erroneous beliefs.

Undergraduate teaching programmes in clinical pharmacology should seek to provide students with a knowledge of the scientific basis of therapeutics. This means instructions in the action, therapeutic effects, toxicity, and fate of the major drugs. Students should also be taught about the relative importance of various sources of information and be introduced at an early stage to their national formulary. They need to know how to evaluate published claims of efficacy and safety, understand the sociology and economics of prescribing, and be adequately prepared for their role as educators of other health care professionals and patients[9]."

The deficiencies in the medical school education that have been recognised by experts can be grouped into three categories:

1. While there is an extensive education in pharmacology and training in making a correct diagnosis, there is little emphasis on how to integrate the knowledge of pharmacology in a clinical situation.

2. Students are not trained how to evaluate information about drugs, which in the absence of systematic ongoing training, leaves them unable to make an objective assessment of new drugs brought into the market after their graduation.

3. Almost no training is offered to the medical students on the humanistic and social aspects of medicine.

Little training in clinical pharmacology and applied therapeutics

Most fresh medical graduates, during their initial independent encounters with the patients, usually are not confident in writing a prescription. They find that they do not have a clear idea of what to prescribe, how to prescribe, and what information they should provide to the patient. In a study done to assess the prescriptions, medical graduates chose an inappropriate or doubtful drug in about half of the cases, wrote one-third of prescriptions incorrectly, and in two-thirds of cases failed to provide important information to the patients[10]. An important reason for this deficiency in prescribing skills of the fresh graduates is that they have not received any structured training in clinical pharmacology and applied therapeutics in their medical school education[1-3] (Box 2).

Pharmacology is an essential component of the undergraduate curriculum. It is usually taught in the second or third year of medical school, when the student hardly has any knowledge of diseases or has seen patients. Teaching is didactic and emphasizes basic pharmacology rather than therapeutics[3]. It aims at transfer of knowledge about drugs rather than training students to treat patients in a rational way[2]. The material is 'drug centered' focusing mainly on issues like: mechanism of action, indications, and side-effects of different drugs. Applied issues like how age, gender and socioeconomic characteristics can affect the choice of drug, significance of cost-effectiveness in therapy, importance of compliance and factors influencing it,

and significance of giving relevant and essential information to the patient are not given much importance in this training[10].

Box 2: Knowledge about therapeutics.

Modern medical education has not dealt as effectively as it should with the education of physicians in therapeutics. A traditional emphasis on the critical importance of diagnosis has not been followed by appropriate concern with the problem of therapeutics.....

The American College of Physicians recognizes that the "drug revolution" provides physicians with the opportunity to treat patients more safely, rapidly, and effectively than ever. To take full advantage of the potential benefits new developments in drug therapy offer to patients, and simultaneously to control the potential dangers these developments offer, the American College of Physicians recognizes the need for improved education of physicians and other health care professionals in rational therapeutics.....

Virtually all formal pharmacologic education occurs in the second year (third year in Pakistan) of medical school, before significant exposure to clinical medicine. In this context students are taught about drugs that are used to treat diseases with which they have only passing acquaintance, and have never seen in clinical situations. This often amounts to giving students solutions to problems they have yet to recognize exist

While this early training in pharmacology is essential to medical education, subsequent education in clinical medicine needs to pay greater attention to inculcating in future physicians the basic principles and important facts necessary for rational therapeutics. This goal may be achieved by developing formal courses in clinical pharmacology and therapeutics in the last two years of medical curriculum, or by incorporating more formal discussions of basic therapeutics into existing clinical programs. Students need to be taught in the clinical context about the rational use of drugs. This instruction should provide a familiarity with the clinical relevance of important pharmacokinetic concepts, an understanding of the need for individualization of drug dosage, an awareness of particular patient populations where drug therapy may be especially difficult, an understanding of the decisive importance of clinical trials for evaluating new therapeutic techniques, and a wise scepticism of pharmaceutical industry claims.

House officers are just equally in need of educational programs in therapeutics. Frequently they are poorly informed about basic laws governing prescription and distribution of medications, and about basic elements of adequate prescription writing..... Like medical students, house officers need to continue to learn basic pharmacological principles, further develop their ability to evaluate clinical trials, and gain a better understanding of the role of drugs in our society and in the physician-patient relationship...

Reproduced from: Meyer BR. Improving medical education in therapeutics (a paper developed for Health and Public Policy Committee, American College of Physicians; Philadelphia, Pennsylvania). Annals of Internal Medicine. 1988;108:145-147.

Clinical training of undergraduate students also concentrates on diagnostic rather than therapeutic skills. A traditional emphasis on the critical importance of diagnosis

is usually not accompanied by equal emphasis on developing the best therapeutic plan[1,11]. Sometimes students are only expected to copy the prescribing behaviour of their clinical teachers, or follow existing standard treatment guidelines, without explanation as to why certain treatments are chosen[10]. Adding to the problem is the fact that prescribing practices in teaching hospitals, that inevitably serve the role model for students, is often irrational and inconsistent, as has frequently been described from developed and developing countries[1].

The irrational prescribing habits once developed are difficult to get rid of or to modify later on[2]. Research shows that despite gain in general experience, prescribing skills do not improve much after graduation. So good training is needed before poor habits get a chance to develop[10]. Therefore, it has been suggested that the principles of rational prescribing should be reinforced in the clinical phases of training[1,2]. According to the World Health Organization: "Although the impact on rational drug use will be long-term, improved undergraduate education in clinical pharmacology is likely to be one of the most cost-effective ways of improving prescribing[9]".

No training on how to evaluate information about drugs

There has been an explosive development in the field of therapeutics during the last few decades. The pace of development has been specially fast in the field of pharmacotherapy. Now we have hundreds of drugs to treat many conditions that once had been of fatal consequences. Knowledge about diseases and their medicinal treatment is still growing and improving. Many new drugs and numerous new preparations are brought into the market each year and experience with existing ones expands. But being dazzled by this rapid advancement, we have not remained sensible about drugs. We use too many drugs and expect too much of them[12]. The situation has been exploited by the manufacturers of the pharmaceutical products. Now, many new drugs are brought into the market even when they do not offer any significant advantage over the existing therapies. They are promoted by the manufacturers simply to earn some profit. Aggressive campaigns are waged to change prescribers' habits and distinguish the product from the existing and competing ones even when they are virtually indistinguishable. False claims based on imperfect trials are made regarding their efficacy and some of these are even promoted for conditions for which they are not indicated[13]. In this scenario, to ensure proper and rational prescribing, it becomes essential for the physicians to remain updated about the advances in therapeutics and have the ability to scientifically and objectively assess any new information about drugs.

However, no training on how to assess information about drugs is offered in the medical schools. Fresh graduates generally are unfamiliar with the various methods of research and are unable to critically interpret statistical data. With this deficiency in their undergraduate education, and in the absence of any formal ongoing training, most doctors face the problem of remaining up-to-date in therapeutics after their medical school education. They do not have any systematic exposure to intelligent, informative, and unbiased assessment of drug therapy. Their continuing education in

therapeutics and pharmacology occurs as the result of random encounters with a variety of information sources, including medical journals, the lay press, interactions with colleagues, and pharmaceutical industry sales representatives. The entire process can be characterized as largely random, incomplete, and subject to distortion[5]. This situation of difficult access to unbiased information on drugs is made worse by lack of any system of compulsory recertification of doctors who, in their busy life, may loose the drive to search for such information altogether.

In this situation, the pharmaceutical industry is an important source of information about drugs. The promotional activities like advertising, promotion through sales representatives, and industry sponsored symposia and conferences provide a major source of continuing medical education about therapeutics. Doctors, throughout the world, have been found to depend upon the information provided by the industry through these means and their prescribing habits are clearly influenced by this information. The information provided by the industry through these means, however, is not always accurate and unbiased because the motive for provision of the information is business. Relying on this information uncritically can adversely influence the therapeutic judgment and prescribing behaviour of physicians (see chapter 8 for details). The predominance of commercial rather than scientific sources of drug information, therefore, has been identified as a problematic area in health care delivery[14].

But many doctors seem to be unaware of this fact and are unable to critically evaluate the information provided by the industry. Some are even unaware of the fact that the information can be misleading. The leading reason for this is that physicians, specially of the developing countries, do not get any training on how to interact with the pharmaceutical industry and how to evaluate any new inform tion on therapeutics they come across.

Teaching medical students and house officers a critical approach to pharmaceutical promotion, therefore, has been emphasized by researchers and experts[15]: They should be explained how marketing works and should be trained to be constantly on the lookout for signs of exploitive tactics employed by the industry that may not be readily discernible[16,17]. They need to be taught to look at advertisements critically. It has been suggested that "immunization against irrational marketing forces could be accomplished by encouraging analysis of advertisements as part of the development of their thought process during undergraduate and postgraduate years[18]". They also need to be taught how to critically evaluate any new information on therapeutics, specially as it appears in pharmaceutical studies and marketing literature[18,19]. It has also been suggested that education about medicines and health should continue beyond medical school so that doctors can get reliable and comprehensive information about drugs that are prescribed[5,20].

No training in humanistic and social medicine

Physician-patient interaction is not a mechanical one. It is an interaction between two humans that involves a great deal more than matching the name of the drug to

the name of the disease. To develop and conduct this interaction effectively the physician not only needs to have a reasonable knowledge about therapeutics, he also needs to have an understanding of the human and social aspects of the interaction. Without such an understanding the therapeutic relationship is likely to remain weak and unstable, and may result in unsatisfactory therapeutic outcome, due to the reasons discussed below:

1. Disease is not an isolated biochemical phenomenon. The conventional biomedical model of disease, therefore, is being replaced by the biopsychosocial model. By having an understanding of the psychological and social aspects of a patient, physician can understand the disease process, and the patient's response to it in a better way and consequently can manage it more effectively (Box 3).

Box 3. The psychosocial component of disease - An example.

A patient suffers chest pain and goes to a hospital emergency room. Because he has had one previous myocardial infarction, he suspects that he is having another. He is examined by a new intern, who also suspects an infarction and who attempts to insert an intravenous line. After several unsuccessful attempts, the intern leaves the patient alone in his cubicle and goes to get assistance. While unattended, the patient continues to feel pain and also feels alone and worried about the competence of his care takers. He suffers a cardiac arrest and is immediately resuscitated successfully by the emergency team.

If the view point adopted by the clinician is a biomedical model based on linear casualty, the successful resuscitation of the patient is a laudable event. If psychosocial factors are taken into account, however, important information is revealed about the patient and the incident; namely, that the patient's pain, fear, and doubts most likely affected the physical disease process, possibly through direct vagal effects, increased levels of circulating catecholamines, or other physiological responses. If medical personnel had considered psychosocial factors and started appropriate treatment - e.g., ensuring constant attention by the nursing staff or using anxiolytic medications - the cardiac arrest might not have occurred at all. The biopsychosocial model does not simplistically assert that the myocardial infarction was a direct result of the patient's psychology. It does provide a broader understanding of disease processes, and it encourages physicians to think about truly comprehensive treatment that considers both the physical and the psychosocial elements of disease.

Reproduced from: Eisendrath SJ. The mind & somatic illness: Psychological factors affecting physical illness. In: Goldman HH (ed.). Review of general psychiatry. New Jersey; Prentice Hall, 1992. p16-17.

2. Culture shapes an individual's response to health and disease[21]. Patients interpret the bodily symptoms according to their personal concerns and cultural beliefs and seek help accordingly. Sometimes harmless symptoms are given too much significance while on other occasions grave symptoms are taken casually due to

cultural beliefs. The way and from whom patients seek help is also culturally determined. There is a strong evidence that patients in every social, economic, and educational class seek and use alternative care[22]. It is, therefore, not uncommon for physicians to come across patients who do not have much faith in allopathic treatment or who are already taking some alternative treatment, while they consult the doctor for help. Similarly, patients also expect different investigative and therapeutic interventions, that are based on the way they interpret their symptoms, in their cultural context. For a physician to develop an effective therapeutic relationship, it is essential that he understands such cultural concerns of the patient. Confronting the patient, irrespective of whether it is overtly expressed or is mentioned in a subtle manner, can lead to discontinuation of therapeutic relationship and failure on the physician's part. Similarly, if the patient's concern for bodily symptoms is not interpreted in the patient's cultural context, the physician can get misdirected in his therapeutic efforts.

3. Patients rely on their physicians not only for skilled diagnosis and effective therapy but also for human recognition of their suffering[23,24]. They expect the physician to appreciate how they feel and what they worry about as sick persons. They also expect that the physician respects them as humans and that he is considerate about their social and financial limitations. An inability of the physician to recognise these and similar humanly expectations of the patient can prove an obstacle to an effective therapeutic relationship.

4. How much reassured a patient feels after consulting a doctor, how much placebo effect is achieved by the physician himself and the suggested treatment, and how the patient complies with the suggested therapeutic advice is also determined by the effectiveness of the therapeutic relationship[25]. If the physician does not have an understanding of the humanistic and social aspects of medicine, the therapeutic relationship will remain weak and therapeutic outcome unsatisfactory in many instances.

5. By understanding the psychosocial dimensions of the therapeutic relationship the doctor can take care of the health of the patient in a broader sense. He can identify the habits and beliefs of the patient that are medically inappropriate and attempt to modify them, without confronting the patient.

Due to these an many other similar reasons not mentioned above, it is important for a practising physician to have an understanding of the humanistic and social aspects of medicine. Unfortunately medical students are not given any training to take care of these aspects of therapeutics. Undue importance is attached to immediate biological causes and social factors contributing to the illness are ignored[6]. An important reason for this major flaw in medical school training is that originally, health education developed along the lines of the biomedical views of health and disease current at that time, according to which social, cultural, and psychological factors were thought to be of little or no importance[26]. Now with the recognition of the role of these factors in health and illness, and in a therapeutic relationship, suggestions have been made by medical education experts to train medical graduates

in these areas (Box 4). It has also been suggested that more attention should be devoted to the development of attitude and skills at the expense of the current preoccupation with technological knowledge[4].

Box 4. Training of medical students in humanistic and social aspects of medicine.

The objective of medical and pharmacy education is to train young persons and equip them with the necessary knowledge and skills to respond to the health needs of the people they serve with care and compassion and to assist these people and the state to achieve their health objectives. During the last three to four decades the number of schools of medicine and pharmacy in the Third World has greatly increased, turning out an increasing number of graduates each year. Many of these schools have maintained high academic standards comparable to those in the advanced industrialized countries. However, the allocation of considerable resources by developing countries in medical and pharmacy education has not resulted in parallel achievements in the field of health care. Obviously, there must be something wrong with the system of medical and pharmacy education in these countries. Many problems have been identified. One of the major problems relates to the need for curricular reforms. Traditionally the learning process in schools of medicine and pharmacy has been subject oriented. There is an urgent need to change this so that the learning process becomes community oriented. In order to effect this change, there must be a proper balance between technological medicine and humanistic medicine. The process of teaching should, therefore, like any other social activity, consist not only of the technical aspects but also simultaneously reinforce social, cultural, economic, and political dimensions as well.

Reproduced from: Balasubramaniam K. Background and objectives of the consultation. In: Balasubramaniam K (ed.). Towards rational drug use - Proceedings of the international consultation on rational drug use in undergraduate medical/pharmacy education; Manila, Philippines; 13-18 August 1988. International Organisation of Consumers Unions. regional office for Asia and the Pacific, Malaysia 1990. p4.

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Chapter 8

Influence Of The Pharmaceutical Industry

The pharmaceutical industry is contributing a lot to human health by searching for and manufacturing drugs. Modern medical services are inconceivable without such an industry. However, the primary objective of pharmaceutical industry, like any other industry, is to produce profit from its involvement in business[1,2] and it is, therefore, primarily interested in promoting the sale of its products[3,4]. As Harry Schwartz, a leading apologist for the US pharmaceutical industry states[5]:

> *"What the industry wants so badly these days - to be valued for its contribution to society - is not what the game is normally about. The pharmaceutical business - like every other business.... is about making money, and it is towards the goal of making the most possible money that industry executives normally devote their energies day in and day out."*

To achieve the business objective of earning the maximum out of their products, the pharmaceutical industry directs extensive marketing efforts towards physicians, pharmacists, administrators[6], and directly to consumers[7]. These marketing efforts exert a significant influence on the prescribing behavior of doctors, which in most instances is adverse and undesired.

The prescribing behavior of doctors who rely on the information provided by the pharmaceutical industry, or who are in interaction with the industry due to other reasons, is specially effected. Such an influence is even more prominent in the developing countries[8] where access to unbiased and complete scientific information on drugs is scarce, governmental control on drug promotion tactics employed by the pharmaceutical industry is lax and most of clinical pharmacology, specially of new drugs, is taught to the doctors by the sale representatives, or journal/magazines that are published or sponsored by the pharmaceutical industry. As a spokesman for the British industry commented[9]:

> *"I would just be talking rubbish if I were to say that the multinational companies were operating in the less developed countries primarily for the welfare of those countries.....They are not bishops, they are businessmen."*

Because the primary ethical obligation of physicians is always to serve in the interest of patients[10], it is essential for them to understand how this influence is exerted and guard themselves against its adverse consequences.

Is influence exerted?

Pharmaceutical companies employe all sorts of marketing tactics and invest huge amounts of money to promote their products. This promotion aims first and foremost to encourage sales[3]. As physicians play a significant part in the sale of their products (by prescribing them), most of these efforts are directed towards them. The aim of any pharmaceutical company, with reference to physicians, is to persuade and influence them to prescribe its products. They are quite successful in this regard. They would hardly spend the amount of money they do on advertisements, symposia, consensus conferences or continued medical education (CME) events unless they believed that their investments paid off in increased profits from the sale of products[11,12]. As Robert C.Noble points out:

> *"No drug company gives away its shareholder's money in an act of disinterested generosity. It is unlikely that pharmaceutical companies are spending $5 million yearly for promotion that isn't effective. Physicians are in fact influenced."*

Pharmaceutical companies have been identified by consumer groups to play a key role in influencing the choice of drugs prescribed[13]. This has been concluded both by pharmaceutical surveys and scientific studies as well[14]. There is a strong evidence that interaction with the pharmaceutical industry influences the prescribing behavior of the physicians[10,12,15-19]. In a recent comprehensive review of 227 papers and about 2000 articles on interactions between physicians and the pharmaceutical industry, Lexchin concluded that there is strong evidence that interaction with the pharmaceutical industry does influence the prescribing behavior of physicians[18].

Detailing, company-funded continuing medical education, and "all-expenses-paid" trips to symposia, all appear to have a powerful effect on the prescribing behavior of physicians[7]. The detailperson, more appropriately called the salesperson, have specially been identified to exert the influence[10,14]. According to American College of Physicians:

> *"There is considerable evidence to support the efficacy of the personal encounter with a professional salesperson in shaping physicians' attitude towards drugs[20]."*

Physicians tend to deny the influence

Physicians are as susceptible as any one else to obvious and less obvious forms of persuasion. But it has been shown that physicians are not always able to recognize the commercial messages and inputs that ultimately bear on their therapeutic

decisions[15]. They cling to the mistaken belief that they are impervious to the persuasive message from commercial organizations and deny the influence[11,20,21]. As Rawlin noted in 1984[4]:

> *".....few doctors accept that they themselves have been corrupted. Most doctors believe that they are untouched by the seductive ways of the industry's marketing men; that they are uninfluenced by the promotional propaganda they receive; that they can enjoy a company's "generosity" in the form of gifts and hospitality without prescribing its products. The degree to which the profession, mainly composed of honorable and decent people, can practice such self-deceit is quite extraordinary. No company gives away its shareholders money in an act of disinterested generosity."*

In a survey of primary care physicians about their perceptions of the two highly promoted agents, propoxyphene-containing analgesics and cerebral vasodilators, a much more favorable attitude to these drugs was discerned than could be supported by the convincingly negative scientific reports of their value. Yet the same group of physicians claimed to be much more influenced by scientific literature and academic sources than the commercial sources of information. The authors concluded: "Physicians who held advertising-oriented beliefs about the index drugs were generally unaware that they were strongly influenced by non-scientific sources[22]."

In another survey, a large number of residents agreed with the statement that they cannot be influenced by discussions (35%) or the receipt of gifts (57%). This, according to the author, "suggests some naivete' about the influence of pharmaceutical industry on prescribing[7]".

Similarly, a research carried out in Switzerland found a close relationship between drugs that are heavily promoted and drugs that are heavily prescribed. The study concluded that prescribing 'freedom' is something of a myth because although they prefer not to admit it, doctors are clearly swayed by promotional pressures[3].

Why physicians deny the influence?

There are numerous reasons why most physicians deny the influence of pharmaceutical industry on their prescribing habits, the significant ones are:

1. The industry exerts its influence on physicians in a subtle and insensible manner. It employs marketing tactics and utilizes marketing techniques that make it look 'unimpressive' and 'uninfluential'. Under cover of this benign impression it effectively exerts influence that cannot be detected easily.
2. Even when physicians realize that pharmaceutical industry may influence the way they prescribe, they erroneously believe they can resist the influence. Commenting on this belief of physicians, Robert F. Woolard has stated: "There are few beliefs in current medical practice that are held with greater passion than physicians' confidence in their ability to resist the influence of the pharmaceutical industry on their professional behavior[7]."

3. Some physicians do realize that the information provided by industry is unreliable but for practical purposes keep on interacting with the industry, specially the representatives, due to different reasons (Box 1). Such physicians employ the psychological mechanism of denial and 'convince' themselves that they are not influenced by such a relationship. This helps them ward off the anxiety that is a consequence of their discrepant behavior.

Box 1: Why physicians see detailers?

Surveys done over the last 30 years, in Britain, Canada, New zealand, and the United States have consistently shown that 90% or more of physicians see some or all detailers who request an appointment.....

No single reason accounts for physicians' willingness to see detailers. A small minority see them for reasons that could only be described as greed: doctors call up detailers to keep communication open between the drug company offers and their hospital department social fund: some sell the samples given to them by detailers; others use detailers to obtain free medications for themselves and their families. Over 40 per cent of hospital-based doctors admitted that the availability of samples for use by themselves and their family influenced their readiness to see detailers. According to one medical director some doctors see detailers because of the little gadgets that are left behind. "Doctors like new toys to play with", was the way he put it.

Other doctors seem to see detailers out of a feeling of obligation or a sense of courtesy rather than for any thing or information that the detailers have to offer. Doctors may also see detailers because of peer pressure. In one American study, doctors who refused to see detailers were criticized by almost 95% of their colleagues. Interns and residents will see detailers because it represents a change from the usual hospital routine of long hours, few thanks, and even fewer concrete rewards. Detailers treat them with respect, value their opinions, and offer them free lunch. For somewhat similar reasons busy general practitioners often welcome a detailer's visit, because it gives the doctor a chance to relax and talk to someone who is not there with a problem. Some doctors see detailers in order to get samples of a new medication to test its effectiveness. Other physicians use the samples that are left behind by detailers to give to patients who cannot afford to purchase medications. Finally, and probably most importantly, doctors see detailers to acquire information about drugs.

Reproduced from: Lexchin J. Doctors and detailers: therapeutic education or pharmaceutical promotion? Int J Health Services. 1989;19:663-679.

How Influence is Exerted

As mentioned above, the primary aim of pharmaceutical industry is to promote the sale of its products. To achieve this it invests between 15 and 25 per cent of its total budget in promotional activities; the proportion being higher in the developing countries[23]. These activities are directed towards physicians, health administrators, pharmacists, and consumers and serve the means by which the prescribing patterns of doctors are influenced.

The direct methods of sale-promotion commonly used include: direct approach to the doctors, pharmacists and chemists by the sale representatives, provision of printed and audio-visual material to these health workers directly or through mail, advertising in medical journals and exhibition at conferences, supply of free samples and presentation of gifts that range from prescribing-pads, pens, and calendars to computers and sponsored trips abroad. Less obvious forms involve a range of industry sponsorship of professional activities such as scientific meetings, supplements of medical journals, educational material and research[24].

Pharmaceutical representatives

Pharmaceutical representatives personally visit doctors, pharmacists and chemists. Contact with these representatives affects the prescribing behavior of physicians, according to both pharmaceutical surveys and scientific studies[10,14]. They have been called the 'stealth bombers' of medicine that swoop in, change physicians' prescribing habits (better than any journal article or formal educator), and disappear again[17].

Pharmaceutical representatives are recognized by the pharmaceutical industry as "the best and most efficient means of convincing practicing physicians to prescribe certain medications[14]" and have long been considered by drug manufacturers to be the most effective way of drug promotion[19]. They are so effective that the industry spends more on representatives than on actual raw material of its products[14]. Up to 50% of the promotional budget is spent on representatives[7,19] and it is estimated that there is one sale representative for three doctors in many developing countries[25].

The pharmaceutical representatives are employed by the industry to promote the sale of their products by influencing the prescribing behavior of physicians. This intention of the industry is clear even from the advertisements they make when employing detailers (see below for details). Training given to the detailers by the industry also emphasizes to develop salesmanship, and there success is measured by the volume of sale they are able to make[19]. They are also given guidelines how to influence the prescriber and promote sale of the product (Box 2). In the mid-1970s, the Johnson & Johnson teaching manual for detailers emphasized the selling rather than the information-providing side of their work: "*Think salesmen and not detailmen. Delete the word 'detail' from the vocabulary and think selling and sales.*" In the basic training course of Merck. Sharp & Dohme's new detailers, they were told not to get sentimental about the doctor's patients they see because "*this business of ours isn't all sentiment and personal relationships, no matter how grand and true and noble they may be. It is also a business*".

While interacting with a physician, the bottom line message of a pharmaceutical representative, therefore, is "prescribe my drug", which is frequently intermingled with emotional appeals and logical fallacies and is accompanied by a couple of gifts and sometimes, a free lunch[17]. The influence of pharmaceutical representatives on physicians' prescribing pattern can also be inferred from the fact that the more heavily a drug is promoted the more it is prescribed[19].

Box 2. Drug company representatives and sales priorities

SIR- The EC directive on Advertising of Medicinal Products for Human Use (92/28/EEC), which came into force on Jan 1, 1993, (see Lancet editorial, 1992;339:1452), requires that "medical sales representatives shall be given adequate training..... to provide information which is precise and as complete as possible about the medicinal products which they promote". Moreover, the directive makes it the drug company's responsibility to ensure that this requirement is implemented.

Confidential "detail" cards used by sales representatives working for Edinburgh Pharmaceuticals, a part of Allen and Hanburys and thus of Glaxo, suggest that the training received is probably rather different from that which the legislators had in mind. Cards, each of which deals with a specific drug or sales target, all start with a section entitled "Campaign Objectives" printed in bold type. When meeting an otolaryngologist or a hospital pharmacist a prime objective for the representative is to encourage surgeons to endorse (pharmacists to support) "Flixonase for inclusion on the hospital formulary". At meetings with retail pharmacists an objective is "to persuade pharmacists to identify those patients who either purchase OTC [over-the-counter] decongestants or who obtain scripts for other nasal sprays and refer them back to their GP for consideration for an alternative therapy".

After the section on campaign objectives many cards have instructions on business objectives. Representatives are told that the company is involved in a "devices war" and to that end, when visiting a general practitioner, pediatrician, or a pediatric nurse, the prime business objective is to "gain commitment to prescribe the Diskhaler, Becodisks and Ventodisks, for either the next asthmatic child or a named asthmatic child".

Finally, the cards have a section headed "Key Messages" which deals with clinical aspects. Key messages to put over when at a general practice meeting are that "Practice nurses have an important role in identifying children suitable for Serevent therapy" and that "Establishing practice prescribing protocols (including Serevent) for children can lead to more effective use of time by GPs and Practice Nurses".

For many years I suspected that this was a major component of training medical representatives received, but had not imagined that the pitch was so blatant. Is it ethical for a health professional to meet medical representatives knowing that these are their real priorities?

Joe Collier. Drug company representatives and sales priorities. Lancet 1993;341:1031-32.

Advertising

Advertising is an established way of promoting sale of a product and the pharmaceutical industry fully utilizes this mean to influence physicians. Though individual physicians nearly always deny that advertising increases their own prescribing, a relationship has been found between leading drugs advertised and

leading prescriptions filled[26]. A survey of general practitioners showed that doctors rated the impact of advertisements on their practice very low and claimed they gained information from other sources. When they were asked certain clinical questions, however, they produced answers which derived from advertisement campaigns and not from scientific literature[27].

All advertising is inherently misleading[28]. It leans heavily on what has been termed "the strategy of desire[27]". Advertisers, by thorough analysis, unmask the unconscious motives and desires of the potential consumers and then exploit them. In this process they give an 'image' to the product that is distinct from the utilitarian product itself but satisfies the consumers' unconscious desires about it. Photos and drawings are widely used to convey expressions and feelings that can give more information than the written words and help reinforce the image of the product. Through this 'image' advertisers are able to promote the sale of a product. A careful and conscious analysis of advertisements is required to discover the unconscious motives that the advertiser is trying to exploit and readers who pay no conscious attention to the advertisements are liable to be influenced exactly the way the advertiser intended.

Pharmaceutical industry also utilizes these basic psychological principles in their advertisements as prescribers are no different from other 'targets'. They value success, enjoy feelings of competence and self esteem, and are pleased by the gratitude of others. They desire an interesting life, relieved of tedium and nuisances. By contrast, they fear failure and reproach. The pharmaceutical advertising aims primarily at exploiting prescribers' emotions and desires[29] and seeks to establish the simplicity, effectiveness, reliability and power of their products. For the same reason positive attributes of products are presented prominently but negative effects are given in a small print or omitted altogether. They make us believe that selecting their product will make treatment easy: 'Rx 2 b.d. for 3 days' and all will be well. In addition, drug advertisements are more visually arresting and conceptually accessible than are papers in the medical literature, and physicians appear to respond to this difference[15]. Since most advertisements are only glanced at, or half read, their reader will not usually seek to analyze the contents. This gives the image-builder the opportunity to establish the image of his product, along with its name - which is the precise objective of the advertiser.

Gifts and industry-sponsored academic activities

Physicians have been the traditional recipients of the marketing campaigns of the pharmaceutical industry. In this capacity, they have also been on the receiving end of all sorts of promotional "reminders", that come in the shape of gifts, food, hospitality, and industry-sponsored educational activities. Physicians have become so accustomed to receiving these material benefits from the pharmaceutical industry that they now expect them with a 'naiveness' that their prescribing habits are not affected by doing so[7,12,16].

Industry provided "gifts"

Gifts are an important tool employed by the sales representatives to establish and retain relationship with physicians. Provision of gifts has been found to enhance the practitioners' attitude towards the representative. A significant number of physician-pharmaceutical representative relationships seem to be retained because of the gifts provided by the reps. In one study 43% of the doctors disagreed with the statement that they would maintain the same degree of contact with the representatives if no gifts are distributed[7]. So these gifts can be considered an important vehicle by which the sales representatives can gain access to physicians and attempt to modify their prescribing patterns.

The receipt of gifts also produces a norm of reciprocity where the receiver is under obligation to give some sort of response. Under this obligation, the physician becomes favorably receptive to the industry's message, looses objectivity, and is led to respond in the way desired by the gift-giver. It is important to mention here that such a norm of reciprocity is produced not only by accepting large or expensive gifts; small and cheap gifts are equally effective in this regard. In fact, it has been demonstrated that, at least in some settings, small rewards are more likely to alter behavior in the direction desired by the donor than are large rewards[1].

To be their patients' best advocates, physicians must be able to approach each therapeutic decision unfettered by conscious or unconscious obligations. The pharmaceutical manufacturers provide gifts to physicians to oblige them and influence their prescribing patterns, and they effectively do so. That is why these gifts have been termed 'bribes' by some authors, who also have suggested that physicians should not accept them[12,30] (Box 3).

Box 3. Refusing Industry's gifts.

Physicians should not take gifts from the pharmaceutical industry for several reasons. First, the gift is purchased with money their patients spent in the purchase of a pharmaceutical. In effect, by accepting the gift, the physician is paid twice by patients, the second time without the patient's knowledge. Second, the physician is the person who decides what pharmaceutical the patients purchase; thus by accepting the gift from the maker of the pharmaceutical, the gift could be construed as a bribe, a kickback, or certainly an attempt to influence the purchase. That is, after all, the company's intent. Most physicians would be outraged to see a judge accept a gift from a party whose case the judge was hearing. Thus, taking the gift is to risk the impression or even the fact, that the physician's ability to fairly choose a drug is compromised. Many companies, including some in the pharmaceutical industry, have rules against there own employees accepting gifts. Third, as explained by Chren, et al.,accepting a gift establishes a relationship between the physician and the drug company that obliges a response from the physician. Chren points out that the physician's character may be altered by a practice that fosters self-interest at the patient's expense. If the AMA and other medical organizations believe that taking "minimal" gifts is acceptable, why should not taking large, expensive gifts be acceptable as well? Should the amount of gift or the idea of the gift be more important?.....

Reproduced from: Noble RC. Physicians and the pharmaceutical industry: An alliance with unhealthy aspects. Perspectives in Biology and Medicine. 1993; 36(3):376-394.

Industry sponsored academic activities

Industry sponsored academic activities is yet another way the pharmaceutical manufacturers influence the therapeutic judgment and prescribing behavior of physicians. Many medical education activities, from grand rounds in individual hospitals to international medical conferences drawing thousands of practitioners, depend upon financial support from pharmaceutical companies. Review of literature

Box 4. US FDA checklist for sponsored meetings.

A draft concept paper issued by the US FDA on "Drug company supported activities in scientific or educational contexts" sets out a checklist which can help to determine whether a company-sponsored event is independent:

Selection of provider. The sponsoring company should not appear to be in a position to exert influence over the content of the activity through the provider. Company staff or consultants involved in sales and marketing activities should not be involved in the activities.

Independent Experts. The company should play no part in selecting presenters or authors.

Disclosure of financial relationships. There should be full disclosure of the source of funding for any activity, including any financial relationships between participating presenters and the company and between the provider and the company.

Topic. The focus should be on broad aspects of a disease and on a variety of treatments, not on a specific drug.

Number of performances. Symposia should not ordinarily be repeated, as repeated presentations allow companies to judge content and selectively to support presentations of programs favorable to its products.

Drug company involvement. The company should agree not to take part in any activities, including scripting, ghost writing of papers, preparation of audio-visual aids, training of presenters, or targeting of points for emphasis, which might influence the treatment of the topics.

Ancillary promotional activities. The company should agree to not to have any promotional activities near the educational activity, such as participation by sales representatives, promotional exhibits or advertisements in any printed materials disseminated in the program.

Liaison. Liaison with the provider should be through the company's medical or scientific departments by individuals with appropriate scientific or medical training, experience and responsibilities.

Medical writers and articles. "Independent" scientific or educational articles about the company's drugs or directly competing drugs should not be written, ghost written, edited or otherwise influenced by medical writers employed by or working freelance for the company.

Reproduced from: Chetley A and Mintzes B (ed.). Promoting health or pushing drugs?: a critical examination of marketing of pharmaceuticals. Health Action International, Amsterdam. 1992. p32.

on the interaction between physicians and pharmaceutical industry suggests that although physicians rank company-sponsored medical education activities lower than objective sources, such as journal articles, as source of credible information, they still attend such activities[18]. A reason underlying this fact is that companies give all sort of incentives to doctors to attract them to these activities. Depending upon the 'usefulness' of the physician, as they view it, the incentives include free meals, honorarium, recreational activities, and fully paid trip to the activity. In some of these activities promotion is achieved only by displaying and distributing promotional material at the activity site, while in others the whole academic activity, including the lectures and presentations, focuses on promotion of product/s of the sponsoring company or companies. Even when such activities have a neutral and unbiased look, the sponsoring companies have been found to manage to get their 'messages' across to the participants by influencing the selection of speakers and topics[23]. Realizing that the pharmaceutical companies employ various promotional tactics, some of them clearly being inappropriate[31], many developed countries have established guidelines for industry-sponsored academic activities (Box 4).

The other promotional methods mentioned above influence the prescribing pattern of physicians in a somewhat similar manner. That is, they also aim at promotion of pharmaceutical products and persuade physicians to prescribe. One of these methods, promotion targeted at the general public, is increasingly being employed by the industry[7,14] and merits some elaboration.

The methods industry uses to reach general public include; direct to consumer advertisement in media, point of sale displays in pharmacies and medical stores, encouraging articles in popular magazines and newspapers and sponsoring of television and radio programs. Such a promotion reinforces the general message that solution to most health problems is drugs. It also creates unnecessary patient demands and expectations and results in an indirect pressure on health workers to prescribe particular drugs. In 1989, only 45% of 5,000 physicians surveyed said a patient had requested a product by name; the number had almost doubled to 88% in 1992[14]. Finally, in countries where regulations regarding over-the-counter sale are poorly implemented, such a promotion also leads to inappropriate and unnecessary self-medication.

Extent of the influence

Physicians' prescribing behavior is persistently being influenced by the pharmaceutical industry. The pharmaceutical representatives, the advertisements, the gifts and financial aids, the symposia and other industry sponsored academic activities, and promotion targeted at general public, all play a part in this influence. The influence from all these sources, when added together becomes enormous and very significant, specially in view of the fact that physicians generally favor the commercial view of a product than the scientific view[18].

The extent of influence of pharmaceutical industry on prescribing practices of physicians is evident from the results of a survey done in Boston, Massachusetts in the early eighties. The survey was done to study the perceived source of influence on physicians prescribing practices and their beliefs about the use of drugs.

The selected drugs for the survey included cerebral & peripheral vasodilators and Propoxyphene. Messages about therapeutic efficacy of these drugs differ substantially between scientific and commercial sources. The cerebral and peripheral vasodilators are widely promoted by manufacturers for senile dementia and peripheral vascular insufficiency but clinical literature overwhelmingly indicates that they are ineffective for these indications. Similarly, propoxyphene is promoted as an analgesic effective for moderately severe pain, such as that of fractures or major surgery, but the weight of evidence demonstrates that the analgesic properties of propoxyphene are at best equivalent to those of aspirin.

In the survey a sample of doctors was asked how important selected sources of influence (Drug advertisements, sale representatives, scientific literature) were on their prescribing. The answers fell into three categories: very important, moderately important and minimally important. The majority of doctors surveyed reported scientific journals to have very important influence on their clinical judgement and prescribing habits, advertisements and sales representatives, on the other hand played a minor role (Table 1).

This sample of doctors was then asked to respond to a question: "Is impaired cerebral blood flow a major cause of senile dementia?" Response of most of the physicians (71%) was 'yes' (Table 2).

Table 1: Perceived Influence on Doctors' Prescribing

Source of Influence	% Responding Very Important	% Responding Moderately Important	% Responding Minimally Important
Drug Advertisement	3	28	68
Sales Representative	20	26	54
Scientific Papers	62	34	4

Table 2: Answers to the question "Is impaired cerebral blood flow a major cause of senile dementia?"

Answer	% Response
Yes	71
No	14
No Opinion	15

Similarly, when these physicians were asked "Is propoxyphene pharmacologically more effective than aspirin as an analgesic?", almost half of them responded 'yes' (Table 3). The results convincingly establish that a significant amount of influence is exerted by the pharmaceutical industry on the therapeutic judgment and prescribing pattern of physicians.

Table 3. Response to the question "Is Propoxyphene more effective than Aspirin as an analgesic.

Response	% of respondents
More effective	49%
Equally effective	31%
Less effective	20%

The influence has led to numerous prescribing trends that are not in the best interest of patients or the public in general (see below for details). The extent of influence of pharmaceutical industry on clinical decision-making and prescribing habits of physicians can also be inferred by having a look at these prevailing "unhealthy" prescribing trends.

1. The notion "a pill for every ill" stemmed from, and is persistently being promoted by, the pharmaceutical industry. Under influence of this notion physicians tend to prescribe medicines for conditions that are self limiting, have equally (and sometimes even more) effective non-pharmacological remedies, or the course of which cannot be modified by medicines.

2. Many ineffective and useless drugs and irrational combination products are available in the market mainly because they can be sold and not because they benefit the health of the population[32,33]. In fact, as many as 70% of the pharmaceuticals on the world market today are inessential and/or undesirable products[8]. All these drugs are widely prescribed because of the influence of the industry on the therapeutic judgment of physicians.

3. Many new drugs are brought into the market by the industry even when they do not offer any clear therapeutic advantage over the existing therapies, just to earn some money out of them. These newer drugs are also expensive than the existing ones because companies also rely on the widely held notion - not always true - that what is newer is better and is therefore worth more[34]. These newer and costly drugs are prescribed instead of time-tested cheaper ones because they are portrayed by the industry as 'more powerful' and 'more effective'.

4. In developing countries some drugs are promoted for indications for which they are not allowed in the developed countries due to scientific reasons. Physicians, under the influence of the manufacturers, not only prescribe for these 'indications' but on occasions, are even unaware regarding the true indications of

the drug. For example, how many physicians are aware of the fact that promotion of cyproheptadine as an appetite stimulant has been disallowed in USA (its country of origin) since 1971 - only one year after its discovery!

Is the information provided by Pharmaceutical Industry reliable?

Pharmaceutical industry is a major source of information about drugs and continuing education about therapeutics[15,35]. The information is readily available, is attractive, and easy to digest. However, the information provided by the commercial sources is usually and significantly biased[1,36-38]. Surveys have confirmed "the marketing of pharmaceuticals without complete information essential for their safe use". Double standards of promotion are commonplace, especially in the provision of information between industrialized and the Third World countries. The benefits of drug use, or attributes that can give it a marketing edge, are routinely emphasized and over-emphasized; and the disadvantages are routinely played down[21]. In developing countries multinational drug companies promote their products in ways that would never be allowed at home[39].

This is something to be expected. The underlying purpose of medical information, particularly data on therapeutics, provided to physicians from commercial sources is, understandably, to promote product sales[22,36], not to supply a balanced, unbiased, or objective view of scientific data. It has been shown that physicians who rely on the pharmaceutical industry for information about drugs are less rational prescribers[1,8]. Relying on the pharmaceutical industry as a source of advice about drugs, therefore, is inappropriate[22]. In all instances where medical information is provided to physicians under commercial sponsorship, physicians are ethically obligated to recognize the potential bias inherent in medical information linked, however indirectly, to commercial drug promotion. The World Health Organization recommends that information about drugs from commercial sources should not be used in isolation from more objective sources[40]. Similarly a well known textbook of pharmacology comments: "The pharmaceutical industry cannot, should not and indeed does not purport to be responsible for the education of physicians in the use of drugs[41]".

Pharmaceutical representatives as a source of information

Relationship of a pharmaceutical company and doctor is maintained through the pharmaceutical representatives. They serve an important source of information dissemination for the industry. They, however, are employed by the pharmaceutical companies to promote the sale of their products, not to educate the doctors or provide them with a balanced information about drugs[1,19] (Box 5). If detailing gives valuable pharmacological information, it is often only a by-product, used as a method of selling.

This role of sale representatives is demonstrated by the wording of advertisements made for their recruitment. These advertisements include statements like "the successful applicant will have demonstrated a successful sales history.....a medical or scientific background would be an advantage but is not essential[1]. In one study of such advertisements it was found that in none of the advertisements was there any emphasis on the importance of detailing to the health services or for patients' health[19]. In only four of 91 advertisements was knowledge of drugs was mentioned as constituting an advantage. Training in commerce was considered suitable in many advertisements. The training given by the employer, the good salary, and a company car, even for private use, were emphasized. Nowhere do the advertisements made any mention of providing information to doctors.

The training given by the industry to the sale representatives also emphasizes to develop salesmanship (see above) and focuses on how to be convincing in there presentations. They are also guided to see physicians who are most likely to increase the sale of companies' products. This mission of detailperson is clear from the blunt statement of one of the former medical directors of Squib[19]:

> *"The primary purpose of the detailmen is to make a sale, even if it involves irrational prescribing and irrational combinations."*

Box 5: Doctors and detailers - Therapeutic education or harmaceutical promotion?

Abstract

Pharmaceutical companies in industrialized countries generally view detailers as the most critical element in the promotion of their products, with the result that over 50% of expenditures on promotion are devoted to detailers. Publicly the companies make claims for the scientific knowledge of detailers and for their role on passing on information to physicians, but the main purpose of detailers is to sell their company's products. This emphasis on sales is evident from statements of detailers themselves, from advertisements for detailers, from company documents, and by looking at the groups of physicians that companies specially target for visits by detailers.

A variety of explanations are offered as to why physicians see detailers, but on examination none of the reasons is justifiable. Studies from a number of industrialized countries have shown that over 90% of physicians see detailers and a substantial percentage rely heavily on detailers as source of information about therapeutics. Detailers are highly successful in altering physicians' prescribing habits, but almost all the literature shows that the more reliant doctors are on commercial sources of information, the less appropriate they are as prescribers. Widespread use of DES (diethylstilbestrol) and the Dalkon Shield was encouraged by detailers. Although detailers have received the endorsement of both physicians' groups and government bodies, seeing detailers is detrimental to the practice of good medicine, and the best interest of doctors and their patients would be served if physicians had nothing further to do with detailers.

Reproduced from: Joel Lexchin. Doctors and detailers: therapeutic education or pharmaceutical promotion (Abstract). International Journal of Health Services. 1989;19:663-679.

Pharmaceutical representatives are given training for the products they are to promote but their knowledge is not always adequate for them to fulfill their role in transmitting information about therapeutics to physicians. A Director General of WHO has focused attention on the problem that sales representatives "often have inadequate medical and scientific training, insufficient knowledge of the actions of the products they promote and of the comparative safety and efficacy of competitive products[29].". An analysis of the information from representatives found that one in 10 statements - all of which favored their product - were at odds with the companies own literature.

In another study 210 drug presentations of sales reps were analyzed[42]. According to the results, the information from sales reps is far from accurate, particularly when side effects of a drug are discussed:

- The indications of drugs were similar to official ones in 77% of the presentations. In 23%, the indications were extended or changed.
- The dosage corresponded to official one in 88% of presentations. In the remaining 12% it was higher, never lower.
- Side effects of drugs were mentioned in only 29% of the presentations. Even when doctors asked about side effects, the sales reps did not always want to answer, or could not.

The representatives are also likely to be left uninformed about some effects of the products that if passed on to doctors might result in a reduction in prescriptions of those drugs. As an Australian sales representative who worked for two multinational companies for a total of four years states[43]:

> *"I do not think reps intentionally mislead doctors as a general rule. I think they are just reflecting the training they've received. They are given selective information themselves because companies, in order to maintain motivation, only want them to know real positives."*

Pharmaceutical representatives also provide the industry a mean to promote drugs for conditions that cannot be mentioned in promotional material due to lack of substantiating scientific evidence. Any such information is clearly misleading and an important cause of inappropriate prescribing but is beneficial to the industry. As a former Squib medical director pointed out[44]:

> *"The incidence of disease cannot be manipulated and so increased sales volume must depend at least in part on the use of drugs unrelated their real utility or need."*

Finally, as the success of the sales reps work is measured by the volume and sales and not by improvement in the knowledge of physicians[19,43], they are only concerned with selling their products. To achieve this, they are likely to mould the information according to the physicians taste and desires or just focus on the information that is

attractive for that particular physician. Sometimes, just to ensure that their product gets prescribed, they can even make an awful advice[45]:

> *[In Bangladesh, a Hoechst detailer was observed trying to persuade a doctor that Lasix was a good drug to use for children who had kwashiorkor or marasmus. These are diseases that result from severe protein deficiency and on of their manifestation is edema or swelling throughout body. Lasix which is a diuretic or 'water pill' is used to eliminate excess fluid in the body. When it was pointed out to detailer that the swelling might go down if Lasix was used but the child would be killed, the detailer responded "Well, the child is going to die anyway."]*

Detailers, as discussed above, are an important source of information about drugs to doctors. Doctors rely on the detailers for such information and are likely to take it uncritically. However, relying on this information has been found to lead to less appropriate and irrational prescribing behavior[1,18]. Joel Lexchin in his study on detailers concludes:

> *"I believe that seeing detailers [sales representatives] is detrimental to the practice of good medicine and that the best interest of both doctors and their patients would be served if physicians had nothing further to do with detailers."*

Information provided in advertisements

Advertising is another important mean by which pharmaceutical industry provides information to doctors. Advertisements are made in various medical journals or provided to doctors in the shape of brochures and pamphlets. These advertisements, however, are made to attract attention to brand name and promote product sale, and do not provide adequate and objective information about the products.

A comprehensive study has been done by an international group to evaluate the information content of advertisements for medicines made in medical journals[26]. A total of 6,910 advertisements were evaluated in this study; 5711 advertisements from 283 separate issues of 14 medical journals in European countries and 1199 advertisements from 60 separate issues of 9 medical journals in developing countries. Important findings of this study are:

- As expected, the ads seem mostly to aim to attract attention to the brand name.
- The advertisements analyzed contained relatively little information.
- Indications were mentioned much more often than the negative effects of medicines.
- Many ads lacked clinically important information on contraindications, adverse effects, and warnings and precautions.
- A significant proportion of ads from most of the developing countries surveyed gave misleading information.

- Over all, the informative quality of ads in the developing countries was poor as compared to the European countries (Table 4).

Table 4. Comparison of content of advertisements in medical journals in developed and developing countries.

Type of information	% of ads containing information	
	Developed countries*	Developing countries**
Indications	89	87
Contraindications	61	28
Warnings	55	29
Side effects	64	29

*Denmark, Finland, France, Ireland, Italy, Norway, Spain, Sweden, Switzerland, United Kingdom.
**Brazil, Indonesia, Nepal, Pakistan, Sri Lanka, Tanzania, Turkey, Zimbabwe.

Physicians may look to the advertisements for science on which to base their choice, and marketers will provide it. When the science is scrutinized, though, it has often been distorted by the advertisers. An American survey of 109 advertisements in 10 journals concluded that the distortion was so serious that a quarter should not have been published, and a third should have been revised[27]. It is not unusual for companies to make claims that cannot be substantiated. Appropriate mention of the negative aspects of medication is mandated by law but information about side effects has sometimes been concealed. Such a practice is not a mere aberration. The situation is specially appalling in the developing countries where the regulatory laws to monitor the advertisements either do not exist or are not enforced effectively (Box 6). Yudkin showed that in developing nations serious and even fatal side effects of analgesics, hormones, and antibiotics had been concealed by certain pharmaceutical companies whose drug-promotion efforts, furthermore, did not always coincide with the medical needs of the countries involved[46]. In analyzing the information supplied by six manufacturers to substantiate claims made in advertisements, the Medical Lobby for Appropriate Marketing (MaLAM) found that out of 67 studies, only 31 provided original data relevant to the questions asked. Of these 31, only 13 were controlled studies, and only 3 were randomized double blind studies. Even these had one or more serious flaws, leading MaLAM to conclude that none of the companies supplied clinical trial reports that both were scientifically valid and supported the advertising claims[28ii].

The advertisements handed over to physicians as brochures and pamphlets may also contain figures, graphs and charts, highlighting certain aspects of the drug (that are always positive!). These results are usually based on the results of company funded clinical trials and are of doubtful validity. The company funded comparative efficacy trials are initiated by the companies who control the data and decide whether or not to publish, and what to publish[47]. Since the sponsoring company retains the rights to

publish the results of any study they fund, clearly, they do not submit for publication the results of a trial that reflect unfavorably on their product[11,48]. Commercial sponsorship of trials, and selective publication of the results, tends to overemphasize the usefulness of drugs.

Box 6. Drug advertisements in developing countries.

SIR, - At a recent meeting in Pakistan, I was told that the urban poor, suffering from diseases associated with overcrowding and polluted water, spend much of their small incomes on useless or inappropriate medicines. Not all of these are "quack medicines" provided by native healers. Some of the worst examples of quackery can be found in advertisements by ethical multinational pharmaceutical companies, taking advantage of the fact that drugs can be easily bought from pharmacists and that local drug-control legislation is weak or ineffective.

For example, many advertisements for benzodiazepines are untempered by western experience. Sandoz assures that "with Restoril (temazepam) patients do not experience drug dependence". Parke Davis states that "Verstan (prazepam) may provide an advantage in certain patients prone by history to drug misuse". Searle announces that "Tranxene extends a helping hand to your worried patients", while Roche claims that 'Lexotanil' (bromazepam) "resolves anxiety and relieves the strain on the heart.... Clinical reports [none of which are listed] confirm that very good results are obtained in angina pectoris, cardiac arrhythmias, palpitations and precordial pain mimicking angina pectoris". These are misleading statements. There are also claims for other drugs which are not part of the UK pharmacopeia. If these claims are correct, then British doctors and their patients are missing out on a therapeutic revolution.

'Loftyl' (buflomedil), according to Abbott laboratories, "alleviates symptoms of intellectual deterioration, change of personality, and loss of memory". 'Sermion' (nicergoline) "revitalizes cerebral circuitry", and is indicated for "intellectual, affective, behavioral and somatic symptoms associated with cerebral decay (including Parkinson's disease and senile and presenile dementia) as well as for memory disorders, reduced concentration, mood depression, unsociability, loss of self-care, asthenia, anorexia and dizziness". This drug is marketed by Farmitalia Carlo Erba, who state that there is only one contraindication - hypersensitivity to nicergoline. I was told that advertisements for these and similar drugs were to be translated into Urdu and aimed at parents who might be anxious about their children's performance at school.

Not all companies behave in this way. I saw several advertisements providing the sort of information that would be required in the UK. The companies concerned included Wyeth, Glaxo, Reckitt and Colman, and Ciba-Geigy.

What can be done? Proposals for a limited WHO list seem doomed to fail in the open market and bazaar. Drug companies will weep a few crocodile tears and carry on until effective local legislation arrives to control them.

Reproduced from: Birley JLT. Drug advertisement in developing countries. Lancet 1989;i:220.

Furthermore, there has been found a significant statistical association between the source of funding and the outcome of the study, with a company funded trials showing more favorable results for a product than non-industry sponsored trials[18]. The author of this study offered three non-mutually exclusive hypotheses to explain this association: industry selects drugs likely to prove efficacious, study results are flawed because of type II errors (sample not large enough), and researchers fear discontinuation of funding should studies show that the drug being investigated is no better than, or inferior to, traditional therapy.

The drug trials referred to in the advertisements are often seriously flawed and tend to be designed to show products in the best possible light. In most clinical trials, the sample sizes are too small and the length of treatment too short to substantiate the claims made on the strength of them. Information from tests and trials on drugs, therefore, typically ranges from inadequate to appalling. It is largely generated by the sponsoring company for use in promoting its products[21,39].

Similarly, indications mentioned or claims made in an advertisement are, sometimes, supported by references from authentic and well known books of pharmacology, medicine, or the specialty to which the product belongs. When these references are looked for in the cited book/s, one may find that the references have been selectively reproduced. That is, the portion of the text that substantiate the claims are reproduced while portions that warn against the use or mention some undesired effect of the compound, whether cited in the same section or some related section, are omitted altogether. Consider, for example, the portions of an advertisement reproduced in Figure 1. This is an advertizement for a fixed-dose preparation that is promoted for "prompt & effective relief of fever, common cold, cough, nasal decongestion, headache, bodyache, sneezing, sinusitis, watery eyes, and general discomfort." The references are cited from an authentic textbook of Pharmacology but their analysis reveals:

1. In the referred to book, the references regarding Chlorpheniramine reads: "These (Chlorpheniramine and other H_1 antagonist alkylamines) are among the most potent H_1 antagonists. The drugs are not so prone as some H_1 antagonists to produce drowsiness and are among the more suitable agents for daytime use; *but again a significant proportion of patients do experience sedation. Side effects involving CNS stimulation are more common in this than other groups*[49]."

2. Similarly, the second reference cited regarding Phenylpropanolamine completely reads: "*Oral decongestants are much less likely to cause rebound congestion (as compared to topical decongestants) but carry a greater risk of inducing adverse systemic effects*[50]."

3. *Finally, and most importantly, the referred to book nowhere recommends the use of such a "multi-purpose" fixed-dose preparation.* In fact, the preparation does not meet the scientific criteria of a combination product and belongs to the group of

FIGURE 1. Though the references for the efficacy of the ingredients of this combination product have been quoted from an authentic book of pharmacology, they are partly reproduced (see text). The product, like most of other similar products, even does not meet the American Medical Association criteria of combination products.

preparations referred to as "less acceptable" and "undesired" preparation (see chapter 10 for details).

Adverse consequences of the influence of pharmaceutical promotion

Promotional activities of pharmaceutical industry are directed towards all levels of health professionals and the public in general. The consequences of these activities are, therefore, multiple. The major adverse consequence pharmaceutical promotion is that it contributes substantially to misconceptions and misunderstandings about drugs[39] that leads to their inappropriate, irrational, and unhealthy use[23,51,52]:

1. All the promotional activities aim at overemphasizing the usefulness of drugs and act as a powerful inducement encouraging people to see medicines as the key to health[53]. People now heavily rely on drugs to maintain or improve health; use of vitamins to improve physical well-being, use of "brain tonics" to enhance mental functioning, and use of "appetite stimulants" to increase appetite (and consequently physical health) are some such examples. They also rely on drugs for self-limiting and minor ailments and expect the physician to prescribe a few drugs whenever they visit him. Under this "pressure" of patient expectations physicians may prescribe something when, in fact, nothing is needed (see chapter 9 for details). This over-reliance of people on drugs has specially led to grave consequences in many developing countries where people have access to all sorts of medicines and use them extensively and inappropriately by over-the-counter purchase.

2. The notion "Medicines should be prescribed only when they are necessary" has been overshadowed by the pharmaceutical industry's concept, "a pill for every ill". All drug promotion - even the most scrupulous - reinforce the belief that treatment with drugs is more appropriate than without[39]. Under the influence of promotional tactics employed by pharmaceutical industry, and "learning" through the information provided by it, doctors develop irrational prescribing patterns:

   - Drugs are prescribed for conditions which do not require drug therapy e.g., antibiotics for common cold, sedatives for everyday stress, and vitamins for nearly everything.

   - Those drugs are prescribed that have no real scientific evidence of efficacy e.g., "cerebral energizers" for mental retardation, senile dementia, and to improve intellectual performance.

   - Drugs are prescribed merely to satisfy the expectations of the patients e.g., use of vitamins and tonics for numerous non-specific complaints, and antacids and gastrointestinal motility enhancing drugs for non-specific gastrointestinal symptoms.

- In developing countries, numerous scientifically irrational combination products are promoted by the manufacturers because they are an easy source of profit for them. These are undesired products but are extensively used by people by over-the-counter purchase. They are also quite often prescribed by doctors because of their lack of scientific understanding of these products.

  Many new drugs are brought into the market by the industry even when they do not offer any clear therapeutic advantage over the existing therapies. Pharmaceutical companies wage aggressive campaigns to change prescribers' habits and to distinguish their product from the competing ones, even when the products are virtually indistinguishable. This is occurring in many therapeutic classes - antiulcer products, angiotensin-converting-enzyme inhibitors, calcium-channel blockers, selective serotonin-reuptake-inhibitor antidepressants, and non-steroidal antiinflammatory drugs, to name a few[34]. These newer drugs are also expensive than the existing ones because companies also rely on the widely held notion - not always true - that what is newer is better and is therefore worth more. Doctors are often overwhelmed and confused by the volume and content of pharmaceutical promotion and by the lack of comparative evidence to enable them to distinguish between similar drugs or between genuine advances and "me too" drugs[54]. They tend to prescribe these newer and costly drugs instead of time-tested cheaper ones because they are portrayed by the industry as 'more powerful' and 'more effective'.

  In developing countries some drugs are promoted for indications for which they are not allowed in the developed countries due to scientific reasons. Physicians, under the influence of the manufacturers, not only prescribe for these 'indications' but on occasions, are even unaware regarding the true indications of the drug. For example, Pizotifen and Cyproheptadine, two compounds widely used as appetite stimulants in many developing countries, have been primarily developed for use in very specific conditions and are not allowed to be promoted and used as appetite stimulants in the developing countries.

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Chapter 9

Patient And Doctor Factors

Therapeutic interaction, judgment, and decision making is not a purely scientific endeavor. It is a complex interaction between the patient, his family members and others concerned about his well being, and the physician as well. All the individuals in this interaction, including the doctor, have their own set of values and cultural beliefs, social and financial pressures, personal likes and dislikes, and family and professional priorities. In this interaction, the participants also have specific expectations from each other. These individual concerns and expectations of the participants have a significant influence on the therapeutic relationship, and on the therapeutic approach and prescribing behavior of physicians.

Patient Factors

People differ from each other in interpreting their bodily symptoms, attaching significance to them and seeking professional help, mainly because of individual differences in beliefs, resources and constrains (Box 1). Some will recognize particular symptoms and seek out a physician for treatment, at times expecting him to perform certain tests and investigations. Others with similar symptoms, instead of consulting a doctor, may prefer to get some type of alternative care. While still others will attempt self medication or dismiss the symptoms as not needing attention. These individual differences in interpreting the significance of symptoms and consequent health seeking efforts influence their, and eventually the physician's, behavior in a therapeutic relation. An understanding of how specific concerns, resources, and expectations of a patient influence the therapeutic relationship is essential for physicians to plan a rational therapeutic intervention and get favorable therapeutic results.

Patients have a preconceived idea about their symptoms

Whenever a person develops some symptoms he attempts to interpret them on the basis of his knowledge, awareness, and cultural and religious beliefs. He may talk to his family members and friends about these symptoms who in return may contribute to his 'understanding' of the symptoms. Patient's previous experience with similar symptoms or knowledge of and discussion with someone else having similar

symptoms will also add to the patient's interpretation. This effort of a patient to interpret and understand his symptoms helps him to form an idea about his illness and seek any help or intervention that he thinks appropriate. That is why when patients consult someone for professional help they already have a preconceived idea about their symptoms. In fact some patients are so 'clear' about their symptoms that they present with a 'diagnosis'. While this preconceived idea about the illness gives a patient a direction to search for the solution, it can influence and mislead the physician on many occasions:

Box 1. Whether or not a person will seek medical care.

Mechanic has suggested that whether or not a person will seek medical care is based on ten determinants:

1. Visibility and recognition of symptoms.
2. The extent to which the symptoms are perceived as dangerous.
3. The extent to which symptoms disrupt family, work, and other social activities.
4. The frequency and persistence of symptoms.
5. Amount of tolerance for the symptoms.
6. Available information, knowledge, and cultural assumptions.
7. Basic needs that lead to denial.
8. Other needs competing with illness responses.
9. Competing interpretations that can be given to the symptoms once they are recognized.
10. Availability of treatment resources, physical proximity, and psychological and financial costs of taking action.

In addition to describing these ten determinants of help-seeking behavior, Mechanic explains that they operate at two distinct levels: other-defined and self-defined. The other-defined level is, of course, the process by which other people attempt to define an individual's symptoms as illness and call those symptoms to the attention of that person. Self-defined is where the individual defines his or her own symptoms. The ten determinants and two levels of definition supposedly interact to influence a person to seek or not seek help for a health problem.

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1. Sometimes persons become preoccupied with certain bodily functions and view them as symptoms of some malfunctioning due to cultural reasons or the prevailing concepts. In fact some of the cultural believes about body malfunctioning have been vigorously publicized by quacks just to ensure that their practices keep running. It is, for example, not uncommon to come across patients who are preoccupied with the functioning of their gut. They may present with all sorts of gastrointestinal complaints but a thorough inquiry will reveal

that their cultural concern for "undesired" effects of certain foods and "functioning" of liver and gut has preoccupied them with their gastrointestinal functioning. Because patients interpret bodily symptoms in their cultural context and attach significance to them accordingly, on occasions, an unscrupulous inquiry into the symptoms can lead the physician to proceed with unnecessary investigations and treatment. Such patients are more in a need of reassurance and education.

2. The way a patient presents and narrates his symptoms is influenced by his preconceived idea about his illness. He will be concerned about and focus on the symptoms that he thinks are significant, at times missing much more important symptoms altogether. Based on his ideas about the illness he will also expect the physician to perform certain examinations and investigations. He may also have an idea of certain drugs from which he can benefit, some of which he might have even tried before coming to the physician. In view of the fact that patients supply at least 85% of the information required for diagnosis[1], a physician can get misled in his therapeutic efforts if he is unheedful in gathering information from patients. In such a case he is also likely to proceed with the investigations and treatment as desired by the patient for the sake of his satisfaction.

3. If the patient's preconceived idea about his illness and the required investigations and treatment is in obvious contradiction with the medical facts, the physician is likely to dismiss it altogether without considering how important it is for the patient. Some physicians may express resentment towards the patient for his erroneous ideas or ridicule him. Any such response by the physician will leave the patient dissatisfied and result in a poor therapeutic relationship[2].

Patients desire to be free of symptoms and the associated distress

Patients generally interpret their illness and measure the progress in it by the physical, emotional, and social distress associated with its symptoms. They may altogether ignore or pay little attention to symptoms that do not cause distress in any of these areas but show much anxiety and concern for the symptoms that are distressing. They would like to be free of the distressing symptoms as quickly as possible not only because of the associated distress but also because, on many occasions, they will believe that being free of symptoms means being free of disease. So they will 'push' and 'persuade' the doctor to help them get over the symptoms as quickly as possible. This pattern of approach by the patient towards his symptoms may influence the therapeutic response of the physician, at times leading him to make irrational choices:

1. Because of the concern for distressing symptoms, a patient, when presenting to a doctor, is likely to overemphasize the symptoms that are troublesome for him but omit or ignore the others. This may cause a bias in his presentation and mislead

the doctor. Consider, for example, an old patient who seeks a doctor for his cough that does not let him sleep at night. He also is having mild fever off and on for last few weeks but thinks it is just due to his sleeplessness and is not worth mentioning. As a result the doctor misses to work this patient up as a probable case of tuberculosis, relates his cough to his smoking, which he had been doing for last many years, and ends the consultation by prescribing a cough syrup and a multi-vitamin.

2. Concern of the patient or his family members towards certain symptoms may lead the physician to prescribe inappropriate symptomatic treatment with a motive to control the symptoms and please the patient or his/her family members. This appears to be one of important reasons why some doctors still prescribe antidiarrheals to children. (I believe most of them know antidiarrheals are not to be prescribed to children even if they do not know the underlying scientific reason!).

3. Patients concern for symptoms may lead the physician to prescribe for self limiting conditions like common cold that do not need medicines or that have a safer non-medicinal alternative. Symptomatic treatment may also be offered for symptoms that are a result of patient's unnecessary preoccupation with certain bodily functions, irrespective of how much it really benefits the patient. For example, patient may be given antacids and antimotility drugs for his preoccupation with gastrointestinal symptoms ; vitamin E and testosterone for his preoccupation with sexual functioning, and so called 'brain tonics' to improve his concentration and performance in academics.

4. To ensure patient satisfaction by relieving him of his distressing symptoms *rapidly*, a doctor is likely over-prescribe or prescribe in irrational combinations. For example, it is not uncommon to see patients of soar throat receiving one of the latest antibiotics, and patients of rheumatoid arthritis receiving more than two nonsteroidal antiinflammatory drugs simultaneously. With a similar aim, many a times parenteral therapy will be preferred where oral therapy is more appropriate and rational.

5. Symptomatic treatment may be offered to control or revert the symptoms that need a thorough and detailed evaluation or education of the patient and modification of his habits, merely because it offers a rapid control. Improving appetite with 'appetite stimulants' and sleep with hypnotics are common examples of such a symptomatic treatment.

Patients expect investigations and drugs

Investigations are so widely used to confirm (or rule out) a diagnosis, and drugs are so commonly used to treat diseases that, over the years, both these types of interventions have achieved a status of 'therapeutic norm'. Now, when a patient seeks

a doctor for his symptoms he, according to his conception of his illness, expects that his symptoms will be investigated for by specific tests and procedures and then he will be prescribed drugs that will cure him. Doctors, under the influence of these expectations of patients, are likely to get carried away and proceed with inappropriate and irrational therapeutic interventions.

Some doctors proceed with the interventions desired by patients believing that increasing the congruence between patient desires for specific interventions and the interventions they actually receive might result in increased patient satisfaction. But this does seem to be exactly true. In a study conducted on patients of General Internal Medicine, patients who felt they were educated about their medical problems, had an opportunity to express their ideas about the nature and treatment of these problems, and discuss areas of life stress with their physician, were more satisfied than patients who felt they had not received any or all of these types of interventions. In contrast, patient perceptions about receiving examinations, tests, medications, or non-drug treatment were only minimally associated with levels of satisfaction with physicians[3].

Doctors prescribe to please the patients

People everywhere share a need to believe in the healing powers of someone or something. Most of us will readily believe in the power of a drug and in this there is little difference between an educated Westerner and a poor, illiterate man or woman. All medicines, whether traditional herbal remedies or modern factory produced drugs, have a special mystique[4].

People want to get well when sick. They want to get well soon. They tend to over-estimate the benefits of drugs[5] due to multitude of reasons, believing that they can offer them complete and rapid cure. So they rely on them when sick. They will take them on their own by over-the-counter purchase or on the recommendation of friends and relatives, and will expect to be prescribed a few when they consult a doctor. The desire to take drugs is, therefore, an outstanding component of health-seeking behavior in all human communities[6], that has been recognized by William Osler as long as a century ago:

> *"But know also, man has an inborn craving for medicine...the desire to take medicine is one feature which distinguish man the animal, from his fellow creatures. It is really one of the most serious difficulties with which we have to contend....The doctor's visit is not thought to be complete without a prescription."*
> (William Osler 1894)

The expectation by patients that the doctor will prescribe drugs puts doctors under pressure to prescribe. Though the pressure may be less than doctors estimate, they respond to it. Sometimes physicians are even unaware of this pressure. In a study on whether patients' demands and expectations influenced the choice of drug prescribed, it was found that though more than half of the sample of doctors (53%)

denied that patient pressure influences their prescribing, the prescribing choice of the vast majority of them (84%) was in fact being influenced by patient pressure[7].

Doctors often prescribe mainly to please patients, rather than cure them[8]. That is why they may prescribe something even when nothing is needed. In this 'nice gesture' towards the patients, physicians are also likely to prescribe more drugs when fewer can do the job and costly ones instead of the equally effective cheaper ones. Such an unscientific response by doctors toward the unrealistic expectations of patients has been recognized to be an important reason of irrational use of drugs. It is also an important contributor to messing up the health delivery services of many countries, as has been commented upon by an expert[9]:

> *"We are not sensible about drugs. We use too many drugs and expect too much of them. We have been dazzled by the relatively few really effective products that have emerged mostly in the last 50 years. But instead of accepting these gratefully and recognizing their limitations, we use drugs as if they could provide an answer to all our ills... This expectation is foolish but understandable, since we all fear sickness and pain. But it has led us, our doctors, the drug manufacturers and our governments into a mess of which no one can be proud. Our credulity as patients, and its legal exploitation by drug companies, are turning doctors into a conduit for drugs to patients - not of course all doctors, not all patients, nor all drug companies - nor all the time. But the phenomenon is real, widespread and too well established".*

Patient's ability to communicate

Patient's education, general awareness and ability to communicate also influences the therapeutic relationship and the prescribing behavior of the physician. Some of the important ways this influence is exerted are:

1. Considering the fact that patients supply most of the information required to make a diagnosis, patients who are able to communicate fluently and effectively make the doctor's job of gathering necessary information easy. The chances of missing some important information or misinterpreting the information, and consequently making a diagnostic error, are lesser with patients who are good in communicating than the ones who are poor in this ability. This effect of patient's ability to communicate on the diagnosis made and treatment suggested by the physician becomes specially significant when a doctor, due to different reasons, does not have enough time to spend with the patient.

2. All patients desire to have information about their illnesses and the advised treatment. There is no difference between poorly educated lower-class patients and better-educated upper-class patients in this regard. However, patients who are poorly educated are likely to ask fewer questions leading the doctor to

assume that they have little desire for information[10]. Consequently they are likely to get less information from the doctor about their illness and treatment.

3. Patients who are able to communicate effectively are likely to develop a better therapeutic relationship with the physician than those who are poor in communicating. Because of this better therapeutic relationship, the former are more likely to be advised for the non-medicinal interventions of their illnesses and offered health education than the later.

4. Patients who are difficult to communicate with are likely to misunderstand or confuse the details of the suggested therapeutic regime. This will result in non-compliance in treatment by the patient and poor therapeutic results leading the physician to alter or change the regime frequently[11].

Patient's access to health facilities

Patient's access to health facilities not only determines how rapidly a patient will seek help when sick, it also may influence the physicians therapeutic approach. A patient who does not have an easy access to particular investigation facilities is likely not to be suggested those investigations than a similar patient who has an easy access to such facilities. Therapeutic regime suggested and follow-up visit advised is also going to be influenced by patient's access to the health facility. For example, oral instead of parenteral treatment might be advised to a patient who does not have easy access to some facility from where he can get the injection administered; and longer intervals for follow-up visits are likely to be given to a patient being managed for some chronic illness requiring adjustment of the dose of the suggested medicine if he lives far away from the facility where he has consulted for advice than if he lives near by.

Financial status of the patient

Patient's financial status has an obvious influence on the therapeutic interventions advised by a physician. Patients who are financially affording have greater access to health care, are more likely to receive the more intensive care offered by specialists, and are more likely to undergo invasive procedures[12]. They are also more likely to be advised tests and investigations, and prescribed expensive treatment than those who are non-affording. Many a times, financially affording patients are suggested investigations that are, in fact, not required. These would have been suggested merely because the physician would have thought "there is no harm in doing these investigations; the patient can afford them" instead of "let us do these investigations because they are needed". On other occasions, as discussed above, the physician would have suggested the investigations just to 'satisfy' the patient's expectations - and to satisfy a rich patient's expectations one needs to suggest expensive investigations! Similarly, a financially affording patient would have been suggested some expensive medicine instead of an equally effective and safe cheaper one with a

view "he would not be satisfied with a cheap medicine". There might be many practical constrains in being all rational in such situations, but physicians need to be constantly on a look-out for not letting the financial status of the patient adversely influence their therapeutic plan.

Erroneous cultural beliefs of the patient

Culture has an important contribution in shaping attitudes and responses to health and sickness in any society, irrespective of the level of sophistication[13]. The ideas people have about health and fitness, their beliefs about certain foods and habits, the way they interpret bodily symptoms, from whom they seek help for these symptoms, and what they expect as intervention, all are influenced by the cultural background of the patient.

All cultural beliefs have *cultural* roots and are not necessarily in accordance with the scientifically established phenomenon or principles. While some cultural beliefs of a society have evolved over the years to contribute to its well-being, others are in contradiction with the scientific principles and a likely reason for bad trends and practices in a society. The same holds true for cultural beliefs about health, illness, and treatment. Patients from any culture can have health beliefs that are not in accordance with the principles of medical science and, therefore, are medically erroneous. Patient's expression of faith in such erroneous beliefs can influence the therapeutic relationship and outcome, and the physician needs to be aware of this:

1. Patient's expression of health beliefs that are in opposition with the medical knowledge (or cultural beliefs!) of the doctor can lead the doctor to show verbal or nonverbal resentment towards the patient. This will result in loss of smoothness of the therapeutic interaction and weakening of physician's control over it. In such situations, the patient is likely to loose faith in his doctor which is essential for an effective therapeutic interaction[14] and the placebo effect of the physician, inherent in all therapeutic encounters, will also go weak. The patient is also likely to take the suggestions made by the doctor lightly and not to comply with them enthusiastically. It is therefore recommended that patients should not be confronted for their erroneous beliefs; instead an attempt should be made to educate them.

2. A doctor may be tempted to comply to the interventions desired by the patient that are based on his erroneous beliefs due to financial reasons or contingencies of his practice. At times he may proceed with such interventions merely to satisfy the patient. Being motivated by the erroneous beliefs of a patient, such a response by the physician will not only be irrational, it will strengthen the erroneous concepts of the patient as well.

Doctor Factors

There are two important doctor-factors that determine the therapeutic approach and decision making of a doctor. Firstly, the way he has been trained, and secondly, the way he keeps himself up-to-date regarding the developments in therapeutics. As discussed in chapter seven, the training given in medical schools, even in the developed countries, has been recognized to have many lacunae. It does not emphasize social and applied aspects of therapeutics leaving the graduates deficient as independent practitioners, who in effect are more vulnerable to pharmaceutical industry promotional tactics and social and patient pressures. Physicians, in most countries, also do not have any formal system of ongoing training and their reliance on "education" provided by the pharmaceutical manufacturers, in view of their deficient medical school training, makes them quite vulnerable to adopt unscientific and irrational therapeutic behavior (see chapter 8 for details). Other factors that influence the therapeutic and prescribing approach of doctors are briefly discussed below.

Physician's concern for general health care of patients

A doctor's therapeutic response towards a patient is influenced by the doctor's perception of his commitment as a physician. That is, whether he simply views himself to be responsible to offer medical treatment for a particular condition of the patient or is he interested in taking care of patient's health in a broader sense.

A doctor who merely views himself as a "prescriber" is more likely to rely on drugs to help a patient retain or reattain his health as compared to another physician who is keen to take care of patient's health in a broader sense. The former, because of his "image" of a physician, might resort to prescribing even for conditions that are self-limiting, can be effectively and more safely cured by non-medicinal interventions, can be remedied by health education, or that have psychosocial basis and require reassurance of the patient. He may also search to prescribe "something" to cure non-medical symptoms of cultural or individual significance instead of educating the patient regarding his beliefs; and the pharmaceutical manufacturers, in many instances, will provide him with that "something". Because such a physician concentrates on prescribing, he also is likely not to focus on non-medicinal aspects required for effective therapeutic management of many chronic illnesses.

Medicines offer a lot in the management of many illnesses but they are not a cure or prevention to all of them. Many diseases, specially in the developing countries, have their roots in poverty, unhealthy living conditions, ignorance, and erroneous health beliefs[15-17]. Effective management and prevention of these conditions is not possible with drugs alone and doctors, while managing these conditions, have to focus on other *possible* interventions as well. As a director of one of the major pharmaceutical manufacturing companies points out[18]:

"Drugs are not synonymous with health,.... there are many forces for the promotion of health, including nutrition, education and hygiene. In some parts of the world, these take priority before more sophisticated medicines are brought into play."

Similarly, despite enormous advances in medical knowledge and technology, clinical developments have reduced the incidence of chronic diseases to only a modest degree[19]. Dietary and other life habits have been clearly recognized to contribute to the onset of conditions like hypertension and diabetes mellitus. Identifying individuals who, due to genetic and other reasons, are at risk of developing such illnesses and appropriately educating them can delay their onset. Even individuals who are under medicinal treatment for these conditions require education about their illness and various factors contributing to it for an effective control.

Unfortunately, due to a multitude of reasons (some are discussed below), doctors have become "prescribers" with a little interest for health education of patients[20]. The interaction between patients and doctors has become most inadequate; although the heavy work load may be a contributory factor, negative attitudes and lack of motivation among them seem to be the main problem[21]. Prescription of drugs is simpler and less time-consuming than giving advice or health education; it may also be more in keeping with some patient's perception of what a doctor's role ought to be. The core goal of clinical practice is improvement of general health status and physical, mental, and social functioning of the patients[22]. It is, therefore, important for doctors to realize that their gradual shift to a limited therapeutic role of prescribing medicines makes them less efficient as health care providers. The role of doctors is to take care of the general well-being of patients to a maximum possible extent, and doctors should try to fulfill their responsibilities in this role.

Level and type of practice

Doctor's approach towards a therapeutic situation is influenced by the level and contingencies of his practice due to different reasons:

1. Doctor's dependence on laboratory and other investigations is partly determined by the ease with which he can get them carried out. A physician working in a well equipped teaching institute is more likely to rely on investigations than a doctor working in some remote rural area. The phenomenon is as simple as with any other daily use facility - you have a facility you avail it till you grow dependent upon it. A doctor is also more likely to order investigations if he happens to have some financial motivation for it, for example, if he has a personal laboratory or x-ray facility attached to his practice. In this process whereas physicians in well-equipped hospitals can go for unnecessary and expensive investigations, those far away from these facilities can refrain from them even when they are really needed. Physicians, therefore, irrespective of where they practice, should make a scientifically based objective assessment when suggesting investigations.

2. Private practice settings where fee is charged for each unit of service provided creates perverse financial incentives, as it is put by economists[23]. That is, when additional diagnostic or therapeutic procedures command additional payments; consciously or unconsciously, the doctor is likely to maximize services, even of questionable necessity. Doctors, therefore, are likely to order investigations and other procedures and follow-up visits more frequently when seeing patients in private practice than when they are seeing similar patients in a fixed-salary hospital set-up.

3. If a doctor is practicing in an area where he has to compete with quacks, he is quite likely to gradually give up to the inappropriate and medically erroneous demands and expectations of the patients and adopt the strategies employed by quacks just to ensure that he effectively competes them in his practice (Box 2).

4. Doctors working in teaching hospitals have a better chance of getting exposed to academic activities than those working in non-teaching governmental hospitals or those doing full-time private practice. The later, therefore, are more likely to "forget" what they had learned in their medical school training and acquire irrational therapeutic and prescribing habits under the influence of social and other pressures[24].

5. In some settings of general practice medicines are dispensed or sold to patients by the practitioner himself. In most of such settings the income of general practitioners derives directly from the amount and variety of drugs prescribed, because they charge no separate fee for the consultation itself. Even if they charge a consultation fee it is nominal and the income of the doctor is more dependent on his earnings from the sale of drugs. As a result, there is tremendous pressure on these practitioners to prescribe drugs[21,25].

6. In developing countries, due to a variety of reasons the quality of care provided by a doctor in governmental institutes is likely to be lower than the care provided by the same physician to patients consulting him privately. As has been pointed out by Milton I. Roemer[23]

> *"Since (in many developing countries) public salaries are very low, the doctors doing mandatory service, as well as other government physicians, spend as much time as possible in private practice. In the typical medical post, rural or urban, the public doctor sees all the patients on hand in a few morning hours. Then he hastens to his private quarters, where in an afternoon he can usually earn more than his government salary for a week. Patients soon learn that they will be examined and treated with greater care in doctor's private clinic, so that, if they can afford the price, they see the doctor privately".*

7. The type of medicines prescribed also seems to be influenced by the place where it is prescribed. In hospitals where patients can get medicine free of cost if it is available in the hospital dispensary doctors, for the financial sake of patients, are likely to prescribe drugs available in the dispensary. On the contrary, doctors

practicing privately, specially those practicing as specialists, are likely to prescribe expensive medicines to satisfy the expectations of their patients.

Box 2. Competition with quacks and influence on prescribing habits

Quacks are medical practitioners who do not qualify to practice medicine independently. They have never been through any formal medical training and hence are not officially registered as practitioners. By definition, properly trained alternative care healers are not quacks unless they employ therapeutic techniques in which they have not been trained. For example, a person trained in Homeopathic Medicine or "Hikmat" is not a quack unless he starts dispensing Allopathic medicines, for which he is not trained.

Quacks are common in most of the developing countries. Usually, but not always, they are individuals who have an experience of working in a hospital or a clinic as a member of para-medical staff. They have some familiarity with the names and preparations of medicines and have a passing acquaintance with simple medical procedures like applying dressing on wounds, administering parenteral treatment, and inserting a urinary catheter.

Quacks usually are able to attract a good deal of patients, mostly from uneducated lower to lower-middle socioeconomic class. Due to lack of scientific medical knowledge they share many erroneous beliefs regarding health, illness, and treatment with the people they "serve" who, therefore, feel comfortable while interacting with them. The fee for their "services" is usually somewhat lesser than that of a qualified practitioner and the interventions made by them generally are in accordance with the expectations and desires of the patients. In fact, some quacks earn their living by exploiting the erroneous health beliefs of the patients. Giving aggressive symptomatic treatment, on many occasions by parenteral route, use of steroids to give the patient a feeling of well-being, infusing dextrose-saline to "save the patient from the bad effects of the heat of summer", and injecting vitamin B-complex to overcome "fatigue" and "weakness" are examples of some of the common "therapeutic" interventions they employ to capture patients.

A qualified general practitioner usually has to compete with a couple of quacks for his practice. Understandably this competition is psychologically irritating - a qualified person has to compete with an unqualified person!, and it becomes more so if the general practitioner is unable to attract a reasonable number of patients to sustain himself financially. In this process of competition with quacks, the general practitioner can proceed with the "who cares" attitude and adopt the "means and methods" employed by quacks to attract patients. After adopting this unhealthy way of practice these doctors may feel uncomfortable initially, but as they start getting "rewarded" for it they are likely to stop bothering about it altogether. The general practitioners, therefore, should be consciously at a look-out for any such change in their therapeutic approach.

Prescribing for non-medical reasons

Prescribing is a complex issue and doctors may prescribe for reasons other than the pharmacological effects of a drug. Drugs may be prescribed to maintain patient contact, to satisfy a humane urge to give something to a distressed patient, to terminate a consultation, or because of perceived patient demand[24-26]. As discussed elsewhere, these non-medical reasons for prescribing, on most occasions, do not have much scientific rationale and lead to unnecessary consumption of drugs by the patients, waste of their financial resources, and reinforcement of their unrealistic faith in drugs. Physicians, therefore, should always avoid prescribing for non-medical reasons.

Another important reason why drugs are sometime prescribed is the desire to achieve a placebo effect through them. There is a reasonable amount of evidence to substantiate the efficacy of placebo effect. Placebos have been shown to provide relieve in cases of angina, rheumatoid and degenerative arthritis, pain, hay fever, headache, cough, peptic ulcer and essential hypertension. In a review of 15 studies, (including seven of his own), Beecher found that an average 35.2% +/- 2.2% of 1,082 patients investigated benefitted from placebo treatment[27]. When a physician prescribes to achieve a placebo effect he should take care of following facts:

1. Placebo effect occurs when patients are convinced of the concern of the physician and value of the drug. Therefore a placebo is likely not to work if it is prescribed in a nonchalant manner.

2. While prescribing a single "relatively neutral" compound to achieve a placebo effect may be justifiable, use of more than one such compound or use of even a single pharmacologically potent compound as a placebo does not have much scientific rationale.

3. The placebo effects occur whenever one party convinces another of the value of the treatment, by "pleasing". It effects doctors as well as patients[27]. Doctors' perception of drug effectiveness is influenced by seeing patients "pleased". Under this influence doctors, in spite of absence of any scientifically supporting evidence, are likely to consider certain drugs to be effective for certain conditions. Consequently, they may develop the irrational habit of prescribing those drugs for those specific clinical conditions with a justification "I have personal experience of the effectiveness of these drugs."

Work-load on the physician

Effects of pressure of work on the therapeutic attitude of the physician is very obvious - it leads the physician to "hurry". Under this state of "hurriedness", it is usually difficult for the physicians to develop an effective therapeutic relationship with the patients: Doctor would not be able to take history in detail, omitting some

parts altogether and would also avoid doing the "time-consuming" physical examination in a systematic manner. He would attempt to compensate these clinically disregarded portions by ordering investigations and, because of his uncertainty over the clinical condition, is likely to prescribe a list of drugs that offers symptomatic relieve and covers whatever physician has been able to gather in the short time. Because of the urgency to terminate the consultation, doctors may also not be very lucid in giving instructions to the patients, for example, about the dosage of the drugs. This will leave the patient confused and contribute to his non-compliance to treatment and consequently, result in a poor therapeutic outcome.

Pressure of work also contributes to pressure to prescribe. Prescription of drugs is simpler and less time-consuming than giving advice or health education. Prescription may also be used by the physician to convey to the patient that consultation is over. Longer consultations, allowing explanation and reassurance, could reduce the "quick fix"! of a prescription to end some consultations. But rethinking prescribing, reviewing individual patients, and changing patient expectations all take time, which many physicians do not have[28].

It needs to be reemphasized here that at present interaction between patients and doctors is most inadequate. *Although the heavy work load of health personnel may be a contributory factor, negative attitudes and lack of motivation among them seem to be the main problem*[21]. Doctors are more interested in medical care than in health care of their patients[23] and they may simply act as prescriber of drugs instead of educating and informing the patients even when they have time.

Uncertainty over diagnosis

Nature and understanding of patient's symptoms by the doctor also influence the therapeutic relationship. Doctors are "pleased" when they are able to make a diagnosis with certainty and, as a result, are more comfortable and confident in their interaction with the patient than when they are unable to make a diagnosis confidently.

It is not uncommon for doctors to be confronted with the problem of uncertainty over a diagnosis. The reasons: the doctor may have incomplete or imperfect mastery of available medical knowledge; information provided by the patient might be patchy; clinical presentation might be vague and confusing; a reliable investigation facility might not be in the financial or geographical approach of the patient; or there might not be enough time to wait for the results of the investigations.

The situation of uncertainty over diagnosis is specially common in general practice settings where 50% of the illnesses seen may not admit of a precise diagnosis[29]. An important factor contributing to the situation in these settings is that many patients with emotional problems present with minor and vague physical symptoms to the doctor. According to some estimates, 30% to 60% of all visits to primary care

physicians are motivated by or are consequence of psychological or emotional problems[30,31].

In such situations of uncertainty, the nature of the doctors adaptive strategies will frequently be influenced by the pressure on him and the contingencies of his practice. As it is consoling for a doctor to make a diagnosis which is amenable to therapy, there is very real risk that doctor diagnose conditions for which therapy is available[32] even when he is not certain about the diagnosis. He also will frequently choose to treat rather than to wait and prescribe to gratify patients' expectations who see prescriptions as a "gift" at the end of consultation[33]. All these factors may lead the doctor to an irrational approach towards the situation. Diagnostic uncertainty not only influences the therapeutic choice made by the physician it, on occasions, may also cause the physician to displace his annoyance over diagnostic uncertainty towards the patient and spoil the therapeutic relationship. Doctors, therefore, need to be vigilant in monitoring their prescribing pattern as well as therapeutic behavior when dealing with patients of uncertain diagnosis.

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Section 3

Rational Use Of Some Common Drugs

"Being dazzled by the relatively few really effective products that have emerged during the last 50 years, we have not remained sensible about drugs; we do not recognized their limitations, use them too frequently, and expect that they could provide an answer to all our ills."

Adapted from:"Medawar C/Social Audit. Drugs and world health. International Organization of Consumers' Union. Holland: Gravisie, Bodegraven, 1984. p39-40."

Chapter 10

Antibiotics - Too Precious To Be Wasted

Antibiotics are chemical substances produced by various species of microorganisms (bacteria, fungi, actinomycetes) that suppress the growth of other microorganisms and may eventually destroy them. However, common usage often extends the term *antibiotics* to include synthetic antibacterial agents, such as the sulfonamides and quinolones, that are not products of microbes[1].

Antibiotics are a medical treasure and one of the most important therapeutic discoveries of the medical history. Since the public ability of sulfonamides in 1930s and Penicillin in 1940s, extensive research in the field, and the ability to chemically modify already discovered compounds, has provided us with a long list of antibiotics. Now we have well over hundred antibiotics to choose from and all bacterial infections are potentially curable. The main classes of antibiotics, along with their mechanism of antimicrobial activity, are enlisted in Table 1. Discussion of the pharmaco-therapeutic aspects of all these classes of antibiotics is beyond the scope of this book. However, a brief discussion on some of the applied aspects of the use of antimicrobials follows.

General Principles Of Antimicrobial Chemotherapy

Antimicrobials are perhaps the only group of drugs that, in most instances offer a complete and a rapid cure to a suffering individual. When used carefully and according to scientific principles they are very effective, but when used injudiciously they carry individual as well as social hazards. Physicians, therefore, have a professional and social obligation to use antimicrobials in a rational way. General principles of their use are described below (also see Box 1).

Is there a real need for antibiotic chemotherapy?

Antimicrobials are effective against microbes only but many a times they are suggested for viral infections and febrile illnesses of noninfectious aetiology (see below). To use antimicrobials in a rational way physicians should always ascertain their true clinical need before prescribing them. The practice of suggesting antibiotics

to all patients of fever merely out of habit, or just to avoid a thorough evaluation of the patient is irrational, dangerous, and professionally inexcusable.

Many physicians erroneously associate every fever with a treatable microbial infections and prescribe antimicrobial therapy without further evaluation. It needs to be remembered that all fevers do not have a microbial aetiology. Most instances of fever of short duration, in the absence of localizing signs, are probably associated with undefined viral infections, often of the upper respiratory tract. There are only three common infectious causes of prolonged fever namely tuberculosis, hidden pyogenic abscess, and infectious endocarditis. Noninfectious illnesses can present

Table 1. Main classes of antimicrobials

Class/Examples	**Mechanism of action**
Beta-lactams/ Penicillins Carbapenems Cephalosporins Monobactams	Inhibit bacterial cell wall formation. Bacteriocidal
Quinolones/ Nalidixic acid, Fluroquinolones (ciprofloxacin, enoxacin, lomefloxacin, norfloxacin, ofloxacin, pefloxacin, sparfloxacin)	Inhibit bacterial DNA replication. Bactericidal
Aminoglycosides/ Gentamicin, tobramycin, amikacin, streptomycin, neomycin	Inhibit bacterial protein synthesis. Bacteriocidal
Macrolides/ Erythromycin	Interfere with bacterial protein synthesis. Bacteriostatic/bacteriocidal
Tetracyclines/ Oxytetracycline, minocycline, doxycycline	Interfere with bacterial protein synthesis. Bacteriostatic
Sulfonamides/ Sulfadimidine, sulfathiazole, sulfamethiazole, sulfamethoxazole	Interfere with folate synthesis in bacteria. Bacteriostatic
Trimethoprim/	Interferes with folate synthesis in bacteria (same metabolic pathway as sulfonamides but at a different point; synergic when given together with sulfonamides)
Other antibiotics	
• Chloramphenicol	Interferes with bacterial protein synthesis. Bacteriostatic
• Clindamycin	Interferes with bacterial protein synthesis. Bacteriostatic
• Rifampicin	Inhibits RNA synthesis of bacteria. Bacteriocidal for mycobacteria when given together with isoniazid
• Metronidazole	Its reduction products appear to react with various intracellular macromolecules. Bacteriocidal (and amebicide)

with prolonged fever. The common ones are the collagen vascular disorders and various neoplasms, specially lymphoma. Various types of cancer, metabolic disorders, hepatitis, asymptomatic regional enteritis, atypical rheumatoid arthritis, and a number of other noninfectious disorders may also present themselves as cases of fever of unknown aetiology[2].

Fever is a good indicator of an infection but sometimes an infection may not cause fever but still require an antimicrobial. For example, local and superficial skin infections, that usually are bacterial, may not cause fever but need to be treated with antibiotics. Similarly, sinusitis, specially in children, which lasts for more than 10 days, has a good chance of being bacterial since viral outbreaks usually improve in a week. Fever may not be present but, in this instance, antibiotics are recommended because of the high probability of bacterial cause.

Similarly, the true need of antimicrobials should be ascertained before they are suggested for prophylactic use (see below for details).

Make a diagnosis and identify the most probable pathogen

For any specific infectious disease, the causative organism is almost always the same. The most probable pathogen causing an illness, therefore, can be predicted with a reasonable certainty by making a diagnosis as precisely as possible.

Most of the common infectious disorders have specific patterns of presentation, and are accompanied by specific bodily symptoms and signs. Their diagnosis can usually be made on clinical grounds if the physician is competent and concerned. On many instances, confusion over diagnosis only arises because the physician is in a hurry and is not motivated to clinically evaluate the patient any further than recording his pulse and temperature.

The situation becomes tricky when, in spite of a real effort, a diagnosis cannot be made on clinical grounds. The most appropriate therapeutic intervention in such instances is dictated by factors like severity of the illness under consideration, availability of, and patient's access to reliable investigation facilities, patient's willingness to "wait and see", and the physician's anticipation about the likelihood of complications if a delay is made in initiating the therapy.

In such situations, not infrequently, doctors choose to treat all that they are suspecting by prescribing a list of antibiotics or one of the latest broad-spectrum antibiotic. In some instances, the reason for such an aggressive approach is that any delay in initiating the treatment, or starting treatment towards the single most suspected infection can result in a harm to the patient. But more commonly the reasons are nonmedical: the patient desires to be free of symptoms as quickly as possible; the doctor feels that any delay in relieving the patient of his symptoms might make him switch over to some other doctor; or merely because the physician believes "what the need of all that trouble when a quick and easy solution is there".

Box 1. Guidelines for rational use of antimicrobials.

On many instances the irrational use of antimicrobials stems from physicians' inappropriate approach towards the clinical situation. Not infrequently the approach is:

1. Patient is feverish; he *must* be having an infection.
2. Let us see the throat or may be ask a couple of questions about his urinary system.
3. Throat is slightly congested but in general both these sites seem to be OK!, where else the infection can be???
4. What the use to ponder about the site of infection!
5. Just prescribe a real good antibiotic to take care of the infection wherever it is (Ofloxacin will be a good choice - it will also take care of him if he is developing enteric fever which is getting common in the area; he can even afford it!).
6. There is no harm in suggesting an antimalarial as well; it is the demand of the season!

A rational approach towards the situation would be

1. Patient has fever; let us see *why* he is having fever.
2. Throat is slightly congested; is it the cause of his fever? let us evaluate.
3. There are no other significant systemic complaints. Physical examination is also unremarkable.
4. The fever is there for last four days or so, might be its pattern can yield something.
5. It does not have a pattern indicative of any of the common infections in the area. however, it accompanied a feeling of soreness in the throat which is now improving.
6. Patient most probably has a viral throat infection and is now on his way to recovery.
7. He does not need any drug in particular; saline gargles three times a day and a few doses of aspirin will do the job.

By putting in an effort to find the cause of fever and, if it is due to some infection, the site of infection, a physician can make a diagnosis with a reasonable certainty on many occasions. Once he has been able to do so then he can prescribe an antibiotic that, as determined by the sensitivity pattern of the most likely pathogen, is suitable to the situation and the patient. If there is a doubt about the diagnosis, he can get help of the appropriate investigations, ensuring that any sample for culture and sensitivity is taken before the initiation of antibiotic chemotherapy. Empirical therapy with one of the latest and very broad spectrum antibiotics can only be justified after a sincere effort to make a diagnosis has been unsuccessful, reliable investigation facilities are not within access, or if any delay in initiating the treatment can result in a harm to the patient. Prescribing such an antibiotic or a combination of antimicrobials merely because it is an *easy* way to tackle the situation is not justified and is irrational.

If the patient's condition permits, a reasonable approach towards the situation of uncertainty over diagnosis is to start treatment for the most likely diagnosis and see the results. If a reliable facility is available then appropriate investigations can be sent for meanwhile. While requesting for investigations, it should be ensured that any sample for culture and sensitivity testing is taken before the initiation of treatment. The results of the suggested treatment can be evaluated on clinical grounds and substantiated with the laboratory findings. If the treatment proves unsatisfactory

even after an adequate clinical trial, or if the laboratory results point towards some other diagnosis, the treatment can be changed accordingly.

With severely sick patients, who commonly report in teaching hospitals or, usually get referred their even if they report to a general practitioner or a doctor working in a rural setting, a delay in treatment can result in harm to the patient. In these situations empirical therapy will be required to "cover" all the likely pathogens. Because these institutes are generally well equipped with investigation facilities, all efforts should be made to make a precise diagnosis and/ or identify the causative pathogen. Once the diagnosis gets established, definite antimicrobial therapy can be instituted - a narrow-spectrum, low toxicity regimen to complete the course of treatment.

But unfortunately, even in teaching hospitals antibiotics (like many other drugs) are used inappropriately, as has frequently been reported by numerous studies both from developed and developing countries (Table 2). In all these studies performance was measured against an agreed standard. Overall, as many as 41-91% of all antibiotic prescriptions in teaching hospitals were considered inappropriate. Unnecessary treatment was by far the most common reason for irrational prescribing, followed by wrong duration, misguided prophylaxis and poor selection of the drug[3].

Table 2. Inappropriate use of antibiotics in teaching hospitals

Country	Inappropriate use (%)	Type/department
Canada (1977)	42%	Surgical ward, parenteral antibiotics
	50%	Gynecological ward (id)
	12%	Medical ward (id)
USA (1978)	41%	All inpatients
Australia (1979	86-91%	Prophylaxis
Canada (1980	30%	Paediatric medical cases
	63%	Paediatric surgical patients
Australia (1983)	48%	All departments
Kuwait (1988)	39%	Paediatric inpatients
Australia (1990)	64%	Patients treated with vancomycin
Thailand (1990)	91%	All departments
South Africa (1991)	54%	Gynecology inpatients
	22-100%	Unrestricted antibiotics
Thailand (1991)	41%	All departments
	79.7%	Surgical prophylaxis
	40.2%	Documented infection

Reproduced from: Hogerzeil HV. Promoting rational prescribing: An international perspective. Br J Clin Pharmac. 1995;39:1-6.

While initiating a therapy on clinical judgment, physicians' should keep in mind that because of the problem of antibiotic resistance there is a change in sensitivity of microbes to various antibiotic over the last few decades. The efficacy of different antibiotics, therefore, has not remained that predictable as it used to be. This, however, does not justify use of the latest and broad spectrum antibiotics for treatment of common conditions unless there is clear documentation or evidence of resistant strains. A prudent approach is to start treatment with one of the conventional antibiotics, only after a specimen for culture and sensitivity has been sent for, and then change the treatment if required. If due to reasons susceptibility testing cannot be requested even then treatment should be preferably initiated with some older antibiotic. If the condition does not respond, and after the factors that can cause treatment failure have been looked for (see below), then one of the later antibiotics with a broad spectrum can be used. Treatment in such situations should be changed only after adequate trial, usually 3 days, for over-hasty alterations cause confusion and tend to produce resistant organisms[4].

Selecting the antimicrobial

Optimal and judicious selection of antimicrobial agents for the therapy of infectious diseases is a complex procedure that requires clinical judgment and detailed knowledge of pharmacological and microbiological factors. Unfortunately, the decision to use antibiotics is frequently made lightly, without regard to the potential infecting organism or to the pharmacological features of the drug[5].

The challenge for the physicians is to know when and for what kind of bacteria a particular antibiotic should be prescribed. Choice of antimicrobial follows automatically from the clinical diagnosis because the causative organism is always the same, and is virtually sensitive to the same drug. To make a rational choice, the physician, therefore, has to know about the pathogen that is causing the illness and its susceptibility to various antimicrobials. Once he has solved this part of the problem, he can then choose the drug that is the most selectively active for the situation under consideration, that produces the fewest adverse effects, and that is most appropriate for the patient.

Clinical significance of bacteriostatic versus bactericidal effect

Antimicrobial drugs are often described as "bacteriostatic or "bacteriocidal". Bacteriostatic antimicrobials inhibit the growth of microorganisms. The effect is temporary and reversible. That is, if the microbe has not been completely eradicated, or its growth has not been suppressed enough to help the natural body defence mechanisms to overcome it, it will resume growth and the infection will recur on withdrawal of the drug. The bactericidal antimicrobials cause death of the microbes and are effective even when the infection cannot be eradicated by host mechanisms (see Table 1 for bacteriostatic and bacteriocidal antimicrobials).

In the majority of infections there is no firm evidence that bacteriocidal drugs are superior to bacteriostatic drugs. However, if a patient does not have effective natural body defence mechanisms, e.g., if he is immunocompromised, or if the infection is at a site where these mechanisms cannot effectively work, e.g., endocardium, treatment with bacteriostatic drugs usually results in a relapse as soon as the drug is discontinued. In such conditions bacteriocidal drugs are typically required for cure. On the contrary if the host has adequate defenses and the site of infection permits these defence mechanisms to be maximally effective, a bacteriostatic drug is as good as a bactericidal one in eradicating the infection.

The terms bacteriostatic and bactericidal are relative and not absolute. Sometimes prolonged treatment with bacteriostatic drugs can kill certain microbial populations (e.g., chloramphenicol and meningococci), whereas bacteriocidal drugs may fail to do so (e.g., penicillin G and enterococci). Nevertheless, the classification provided in Table 1 generally holds true.

Clinical significance of spectrum of antimicrobial activity

Based on their spectrum of activity, antimicrobials are either "narrow" spectrum or "broad" spectrum. As the terms suggest, the former are effective against a select few microorganisms while the later are effective against a wide variety of bacterial types. The term "extended" spectrum is applied to antibiotics that are effective against gram-positive organisms and also against a significant number of gram-negative bacteria.

Broad spectrum antibiotics are more likely to suppress the growth of or destroy non-pathogenic bacteria that are part of normal flora and their use can lead to overgrowth of microorganisms that are resistant to the drug being administered. Diarrhoea caused by overgrowth of *Clostridium difficile* in the intestine follows treatment with broad spectrum antibiotics to which this microorganism is resistant. Similarly, after prolonged treatment with broad spectrum antibiotics a secondary fungal infection may occur.

The spectrum of antibacterial activity of the drug chosen should ideally be as narrow as possible, to minimize the detrimental; effects on the normal flora. "Blind" therapy, however, necessitates use of antibiotics with a broader spectrum than required.

Defining the dose, route of administration, and duration of treatment

Successful therapy depends upon achieving antibacterial activity at the site of infection. Hence the site of infection may determine the choice of drug. Physician, therefore, have to be aware of the pharmacokinetic characteristics of antimicrobials that determine their distribution in the body to use them well. Some examples of how these characteristics determine the choice are[6]:

1. Cephalosporins (except third generation members), aminoglycosides, clindamycin, lincomycin, and amphotericin B do not reach the CSF in sufficient amounts to counter infection in the brain or meninges.
2. Erythromycin is only partly excreted in urine and is therefore unsuitable for the treatment of urinary tract infection.
3. Ampicillin, amoxicillin, cephalexin, and rifampicin achieve high concentrations in the bile and hence may be suitable for the treatment of biliary tract infections.
4. Nitrofurantoin attains therapeutic levels only in the urine and should not be used in any infection other than urinary tract infection.
5. Clindamycin and lincomycin penetrate deep tissues and are useful in the therapy of cellulitis and osteomyelitis caused by staphylococci and *Bacteroides fragalis*.

The dose of the drug may also be determined by the site of infection. The eye, prostate, and bone are poorly penetrated by drugs, and infections in these sites require higher dosage of antimicrobials. Higher doses are also required when infection involves avascular tissues, as in bacterial endocarditis and tissue necrosis.

Two important factors that determine the route of administration of a drug are the severity of illness and the site of infection. While oral administration is preferred whenever possible, parenteral administration of antibiotic is usually recommended in seriously ill patients in whom predictable concentrations of drug must be achieved. Once clinical response has been achieved, however, oral therapy is cheaper and safer. Intravenous therapy need seldom be continued for more than 14 days[7], if an oral preparation is available and the patient can be given orally. The route of administration may also vary depending upon where the drug needs to be concentrated. For example, while it may be enough to apply locally for a superficial infection of skin, to achieve high concentration of a drug in the central nervous system it might have to be given intrathecally. The pharamcokinetic characteristics of a drug also determine the route through which it should be administered. For example, aminoglycosides, that are poorly absorbed when given orally need to be given parenterally to achieve systemic effects, but for a local effect in the gut neomycin, one of aminoglycosides, is given orally, and for infections of the skin it can be applied locally as an ointment or cream.

The duration of therapy depends upon the type and severity of the infection. Generally, effective antimicrobial treatment results in reversal of the clinical and laboratory parameters of active infection and marked clinical improvement. However, varying periods of treatment may be required to cure an infection. The duration of therapy required for cure depends upon the pathogen, the site of infection, and host factors. Precise data on duration of therapy are available for a few infections, e.g., streptococcal pharyngitis, cystitis, syphilis, gonorrhea, and tuberculosis. In many other situations, duration of therapy is determined empirically. For serious infections, continuing therapy for 7-10 days after the patient has become afebrile or cultures have become negative is a useful general rule[8]. To avoid untoward effects of the drug and the risk of superinfection, treatment should not be unnecessarily prolonged.

Surgical clearance of infection

The penetration of pus, fibrin, and necrotic tissue by most antimicrobial agents is poor, thus, incision and drainage of abscesses and removal of necrotic tissue is often necessary for successful treatment with antibiotics. When dealing with deep-seated abscesses, although one is often tempted to delay surgery until the patient's systemic symptoms have abated, in many cases the patient will remain ill until essential surgery is performed. However, if the patient is improving and particularly if diagnostic tests (e.g., ultrasonography, CT scanning) show shrinkage of an abscess, then surgery may be postponed[8].

Foreign bodies serve as a "place to reside" for bacteria where they are relatively secure from the phagocytes as well as the action of antimicrobials. Infections associated with foreign bodies are thus characterized by frequent relapses and failure, even with long-term, high-dose therapy with antibiotics. Frequently recurring urinary tract infection in patients having a stone in their urinary system is a common example in this regard. Successful therapy usually requires removal of the foreign body.

Host factors in antimicrobial chemotherapy

To provide maximum therapeutic benefit to the patient and to keep the risks of treatment one has to take into consideration various host-factors as well. These include:

1. A prior history of adverse effects with any particular drug.
2. Metabolic or genetic disorders predisposing to drug toxicity.
3. The status of renal and hepatic functioning.
4. The likelihood of drug interactions.
5. Age of the patient.
6. Pregnancy and lactation.

Prior history of adverse effects

Adverse effects of antimicrobials are conveniently categorized into:

- Hypersensitivity reactions that are not dose related.
- Toxic and irritative effects that are dose related.
- Superinfection.

Whenever an antimicrobial is being selected for the management of an infection, it is important to ask the patient for any prior history of drug adverse effects, specially hypersensitivity reaction. Any history of anaphylaxis or hives and laryngeal edema, or even a skin rash, with a particular drug should be taken a serious note of and the drug (or chemically related one) should not be suggested.

The beta-lactam derivatives (penicillins and cephalosporins) and their degradation products are specially notorious for provoking allergic reactions. Patients with history of atopic allergy seem particularly susceptible to the development of these reactions. The sulfonamides, trimethoprim, nitrofurantoin, and erythromycin have also been associated with hypersensitivity reactions, specially rash. Bone marrow depression induced by chloramphenicol is believed to be an allergic reaction as well.

Metabolic disorders predisposing to toxicity

The most important metabolic disorder with reference to use of antimicrobials is glucose-6-phosphate dehydrogenase deficiency. A number of drugs, including the sulfonamides, nitrofurantoin, chloramphenicol, and nalidixic acid, may produce acute hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency.

Renal and hepatic function

Drugs are metabolized in liver and excreted by the hepatobiliary and renal systems. Depending upon the rout through which they are eliminated (Table 3), the dose of antimicrobials needs to be adjusted (reduced) in patients with hepatic or renal function impairment. Renal and hepatic functions should be monitored when a potentially nephrotoxic or hepatotoxic antimicrobial (or for that matter any drug) is being given to a patient.

Table 3. Routes of elimination of antimicrobials

Primarily renal Aminoglycosides, Cephalosporins, Ethambutol, Nitrofurantoin, Vancomycin
Primarily hepatic Chloramphenicol, Clindamycin, Doxycycline, Erythromycin, Lincomycin, Metronidazole, Rifampicin
Renal and hepatic Most penicillins, Most tetracyclines, Isoniazid, Quinolones

Reproduced from: Abou YZ, Alwan AAS. Guide to chemotherapy and chemoprophylaxis in bacterial infections. WHO, Regional office for the Eastern Mediterranean, Egypt 1993. p15.

Likelihood of drug interactions

The possibility of adverse drug interactions should always be born in mind when a patient is suggested some treatment. The potential interactions of commonly used antimicrobials with various other drugs are summarized in Table 4.

Table 4. Interactions involving antimicrobial drugs

Antimicrobial Drug	Other Drugs	Results
Aminoglycosides	Cephalosporins, cycloserine, vancomycin, amphotericin, fursemide	increased nephrotoxicity
	Loop diuretics, vancomycin	increased ototoxicity
	Neuromuscular blockers	Increased skeletal muscle paralysis
Cephalosporins	Aminoglycosides, probenecid, fursemide	Increased nephrotoxicity
Chloramphenicol	Sulfonylurea, dicoumarol, phenytoin	increased effects of these drugs
Doxycycline	Barbiturates, phenytoin, carbamazepine	Decreased doxycycline effect
Erythromycin	Theophylline, oral anticoagulants, digoxin, phenytoin, carbamazepine	Increased effect of these drugs
Isoniazid	Phenytoin, carbamazepine	increased toxicity of these drugs
	Rifampicin	Increased incidence of hepatitis
	Carbamazepine	Increased toxicity of carbamazepine
	Aluminum antacids	Decreased isoniazid effect
Metronidazole	Anticoagulants	increased anticoagulant effect
	Phenobarbitone	Decreased metronidazole effect
- Penicillins:		
- Ampicillin	oral contraceptives	Decreased effect of contraceptives
	Allopurinol	Increased incidence of allopurinol rashes
- Carbenicillin or ticar - cillin (high doses)	Aminoglycosides	inactivation of glycosides
- Ticarcillin	Lithium	Hypernatremia
- Rifampicin	Oral anticoagulants, contraceptives, oral hypoglycemics, beta-blockers, phenytoin, digoxin, theophylline	Decreased effect of these drugs
Trimethoprim-sulfamethoxazole	Oral anticoagulants	Increased anticoagulant effect
	Phenytoin	Increased phenytoin toxicity
Vancomycin	Aminoglycosides, cephalosporins	increased nephrotoxicity
	Aminoglycosides	increased ototoxicity

Adapted from: Abou YZ, Alwan AAS. Guide to chemotherapy and chemoprophylaxis in bacterial infections. WHO, Regional office for the Eastern Mediterranean, Egypt 1993. p13.

Age of the patient

The age of the patient is an important determinant of pharmacokinetic properties of antimicrobial agents. Mechanisms of elimination, specially renal excretion and hepatic biotransformation, are poorly developed in the newborn and adjustment in the dose has to be done. Sulfonamides should be avoided altogether since they may cause jaundice and kernicterus. Chloramphenicol may cause "grey-baby syndrome" and should also be avoided in newborns.

In patients over 50 years old the rate of renal elimination of drugs is reduced even if blood urea and creatinine concentrations are within the normal range[9]. Hence the dose of potential toxic drugs should be reduced in such patients. Also, elderly patients are particularly susceptible to ototoxic effects of aminoglycosides.

Pregnancy and lactation

Pregnancy imposes an increased risk of reaction to some antimicrobials for both mother and fetus. For example, hearing loss in the child has been associated with administration of streptomycin to the mother during pregnancy. Tetracyclines can affect the bones and teeth of the fetus, and can cause fatal acute fatty necrosis of the liver, pancreatitis, and associated renal damage to the pregnant female. With their reference to safety in pregnancy, antimicrobials have been grouped into those that are probably safe, those that have to be administered with caution, and those that are contraindicated (Table 5).

Another factor to be taken care of while prescribing antimicrobials in pregnancy is that in pregnancy, the plasma concentrations of most antimicrobial agents are lower because of increased total body water, increased liver metabolism, and increased renal plasma flow. Low concentration in the blood and the tissues may lead to therapeutic failure. If this is attributed to the wrong choice of antibiotic, it will be changed unnecessarily. Full doses of the most appropriate antibiotic should always be employed when treating infections in pregnant women, with careful monitoring for side effects[10].

The lactating female can pass antimicrobial agents to her nursing child. Both nalidixic acid and sulfonamides in breast milk have been associated wi.h hemolysis in children with glucose-6-phosphate dehydrogenase deficiency. In addition, sulfonamides, even in small amounts received from breast milk, may predispose the nursing child to kernicterus[11].

Monitoring therapeutic response and terminating the treatment

Like any other treatment, treatment with antimicrobials has to be monitored for the therapeutic response and undesired effects. It will need to be changed if the condition is not responding to the suggested regimen or if the patient has started having distressing or potentially dangerous side effects. When the treatment is being

changed because of a poor therapeutic response it is always prudent to look for any other factor that might be a cause of therapeutic failure (Box 2) before making any change, and make appropriate interventions if any such factor is identified. Similarly, haste should not be made in changing the treatment unless their are clear indications for the inadequacy of the suggested treatment.

Table 5. Safety of antimicrobials in pregnancy

Probably safe: These antimicrobials have demonstrated no important consistent risk. For example,

- Cephalosporins
- Erythromycin (base or stearate)
- Fusidic acid
- Penicillins

To be used with caution: Drugs in this category should be used only for specific bacteriologically proven indications, if a safer alternative is not available, because they are associated with theoretical risks. For example,

- Aminoglycosides (possible ototoxicity)
- Antitubercular drugs (cycloserine, ethambutol, ethionamide, isoniazid, pyrazinamide, rifampicin)
- Chloramphenicol (contraindicated at term)
- Metronidazole (teratogenicity)
- Nitrofurantoin (neonatal hemolysis - contraindicated at term)
- Sulfonamides (contraindicated at term)
- Tinidazole (avoid in first trimester - risk unknown)
- Trimethoprim (possible teratogenesis)
- Vancomycin

Contraindicated: These have defined toxicity and are contraindicated for use in pregnancy. For example,

- Chloramphenicol (aplastic anemia in mother, grey-baby syndrome)
- Erythromycin estolate (maternal hepatotoxicity)
- Lincomycin and clindamycin (maternal pseudomembranous colitis)
- Quinolones (possible arthropathy in the fetus)
- Sulfonamides (neonatal hemolysis, methemoglobinemia and kernicterus)
- Tetracyclines (discoloration and dysplasia of teeth and bones)

Recently developed drugs, with which no experience in pregnancy has been obtained, should also be included in the "contraindicated" category.

Adapted from: Munday AS, Brodie MJ. Antibacterial agents: toxicity and interactions. Medicine International 1992:4383-4391. And. Abou YZ, Alwan AAS. Guide to chemotherapy and chemoprophylaxis in bacterial infections. WHO, Regional office for the Eastern Mediterranean, Egypt 1993. p16.

Adequacy of therapy is usually assessed by clinical response and, if required, is substantiated by appropriate investigations (usually leukocyte count and erythrocyte sedimentation rate). The rapidity of response depends upon a number of factors, including the site of infection (deep-seated infections like endocarditis and osteomyelitis respond slower than superficial infections such as pharyngitis, cellulitis, and cystitis), the pathogen (virulent organisms such as *Staphylococcus aureus* respond more slowly than viridans streptococci, the host (immunocompromised patients respond slower than immunocompetent patients), and the duration of illness (in general, the longer the symptoms are present, the longer it takes to have a response). Thus, depending on the clinical situation, persistent fever and leucocytosis several days after initiation of therapy may not indicate improper choice of antimicrobial but may be due to the natural course of the disease being treated.

Box 2. Causes of failure of antibiotic therapy

Sometimes in spite of the right selection of an antibiotic for a particular condition, even when the antibiotic has been found to be effective during in vitro susceptibility tests, treatment may prove ineffective clinically. In such situations the physician should not make a haste in changing the antibiotic or adding another to it until he has ascertained the cause of therapeutic failure. By identifying the cause of treatment failure and making interventions accordingly he can avoid misuse of antibiotics and unnecessary patient suffering on many occasions. The main causes for the failure of antibiotic therapy are[8,12,13]:

1. The wrong route of administration is used.
2. The host defence mechanisms are not effective, because of either the location of the infection or because of their general impairment.
3. The drug cannot penetrate the site of infection, e.g., brain, eye, prostate.
4. The organism other than the one responsible for infection was isolated (specially in cultures from sputum and throat).
5. An abscess is not adequately drained.
6. A foreign body is not removed.
7. There is delay in the initiation of therapy.
8. The administered doses are suboptimal.
9. The duration of therapy is inadequate.
10. There is development of antimicrobial resistance of the infecting organism.
11. Superinfection by other pathogens have resulted.
12. There is dual infection initially but only one of the pathogens has been detected and treated.
13. The culture and sensitivity report provided by the laboratory was erroneous.
14. The patient is not complying with the suggested therapeutic regimen.

Using Antibiotics In Combination

It is not uncommon to see patients being prescribed two or, at times, even more than two antibiotics simultaneously in the absence of any clear-cut indication (Prescription 1). Such an indiscriminate and irrational use of antibiotics is usually a consequence of:

Physician's uncertainty over diagnosis

Not infrequently doctors, specially the general practitioners, are confronted with the problem of uncertainty over a diagnosis. In such situations they might resort to "treating" all that they are suspecting. If their suspicion is for some form of infection, then just to make sure that nothing is missed, they may "bombard" the microorganisms by prescribing more than one antibiotics to the patient. While on rare occasions such an approach might be justified, practicing it as a routine is irrational and an indicator of prescriber's clinical incompetence or lack of concern for the patient.

An "attempt" to speed up recovery

Sometimes antibiotics are prescribed in combination with a belief that it will speed up the recovery. Combination of antibiotics does offer therapeutic advantage but the combinations are very specific and the conditions for which they are recommended are few. Indiscriminate combinations usually do not offer any therapeutic benefit. In fact, in some instances, the antibiotics included in the combination might antagonize each other resulting in attenuation of their antimicrobial activity. A classical example of such an antagonism is suppression of the bacteriocidal activity of penicillins when they are given in combination with bacteriostatic tetracyclines[14,15].

In general, use of a single antibiotic is the optimal choice. Most infections can be cured by use of a single antibiotic if it is selected correctly, administered in correct dosage by the correct route and is use for the correct duration of time. Their is no rationale for indiscriminate concomitant use of more than one antibiotics. Such a use exposes the patient to unnecessary adverse effects, increases the cost of treatment, and increases the likelihood of the development of resistant strains.

Situations in which combination of antibiotics is rational

When antibiotics are combined rationally they offer great therapeutic benefit. Such rational combinations follow definite pharmacological and microbiological guidelines and are recommended for specific clinical conditions. These are[16,17,18,19].

1. Treatment of mixed bacterial infections.
2. Therapy of severe infections in which a specific cause is unknown.
3. Enhancement of antibacterial activity in the treatment of specific infections.
4. Prevention of the emergence of resistant microorganisms.

Ref. No. _____ Date 11/5/96.

Rx Mirza Irshaad 14.

- Tab. Augmentin 625mg (4
1+1+1
- Tab. Septran (3
1+1
- Tab. Magnapyral (4
1+1+1
- Tab. Fansidar (2

Fe — P. 102 F

B.P. 140/90

HYDERGINE® 1.5 mg 4.5 mg

TERNELINE® 1 x TDS

TAVEGYL® Syp. Tab. ds

PRESCRIPTION 1. The prescriber's rationale of combining Augumentin (amoxicillin + clavulanic acid) and Septran (sulphamethoxazole + trimethoprim) cannot be commented upon. He has also added an antimalarial (Fansidar) to the treatment perhaps just to "ensure" that nothing gets missed.

Use of combination of antibiotics beyond these above mentioned situations is not justified, increases the risk of toxicity and the chance of emergence of antibiotic resistant microorganisms, and is, therefore, irrational.

Treatment of mixed bacterial infections

Some infections are caused by two or more microorganisms. These include intraabdominal, hepatic, and brain abscesses and many of the genital tract infections. In such conditions it often is necessary to administer antibiotics with different antimicrobial spectra to obtain the necessary breadth of activity. To achieve the desired effects , full doses of each drug are needed.

Therapy of severe infections in which a specific cause is unknown

Many a times antibiotic therapy has to be initiated before a specific cause or a causative organism can be identified. Such situations, specially when a delay in initiating the treatment can result in a harm to the patient, demand that a combination of antibiotics should be started to cover all the microorganisms that are most likely involved. The selection of antimicrobials should be based on clinical judgment, a knowledge of the microbiology of the suspected diseases, and an understanding of the antibiotic spectrum of the available drugs. Prescribing a host of antibiotics indiscriminately, with a hope that they will cover every microorganism, might result in more harm than good to the patient and always need to be avoided.

Enhancement of antibacterial activity

Certain antibiotics produce synergism when they are administered together. This effect may permit a reduction in the dosage of one or both drugs with achievement of similar therapeutic effect or alternatively, it may produce a more rapid or complete bacteriocidal effect than could be achieved with either drug alone. There are specific clinical indications for such a combination that are based on documented proof of efficacy. For example, penicillin and gentamicin are synergistically inhibitory to *Enterococcus faecalis* and more effective than penicillin or gentamicin alone in the treatment of *E. faecalis* endocarditis.

Prevention of the emergence of resistant strains

Though in theory combination therapy with antibiotics can prevent or delay the emergence of resistant strains, in reality it is not so. The only valid indication for use of antibiotics in combination for this reason is tuberculosis, where the concomitant use of two or more appropriate agents strikingly reduces the development of drug resistance by tubercle bacillus.

Common patterns of antibiotics misuse

Antibiotics are used indiscriminately, are prescribed for problems for which they are ineffective, and are promoted in a way that may create unrealistic expectations for both the consumer and the prescriber[20]. A considerable medical literature reports that many - perhaps a majority - of antibiotic treatments are medically inappropriate[21]. Their inappropriate and unrestricted use is specially common in many developing countries[22]. Some common patterns of their inappropriate use are:

Treatment of viral infections

Though it is recommended that antimicrobials should not be used to treat viral infections[23],their use for this purpose is not uncommon. In almost every medical community studied, large quantities of antibiotics are administered to patients with viral infections[21]. Their use for diarrhoea and non-bacterial infections is specially common all over the Third World[24]. Antimicrobial therapy of at least 90% of infections of upper respiratory tract is totally ineffective and, therefore, worse than useless[25]. But still they are, not infrequently, suggested for flue, common-cold, and other trivial upper respiratory tract infections. It needs to be appreciated that antimicrobials are not antivirals and do not benefit a patient of viral infection in any way.

Treatment of fever of unknown aetiology

As discussed above, all fevers do not have a microbial aetiology. But many doctors somehow relate every fever with a treatable bacterial infection and prescribe antibiotics. For example, use of antibiotics for treatment of upper respiratory tract infections, that in most instances are of viral aetiology, is not an uncommon practice. Some physicians might plead that they prescribe antimicrobials for minor upper respiratory tract infections to avoid any superimposed bacterial infection. But it needs to be realized that in an immunocompetent person, who takes care of his diet and rest when having a viral upper respiratory infection, chances of his developing a superimposed bacterial infection are not such to justify prophylactic use of antibiotics.

It must be stressed that antimicrobials are not antipyretics. The most rational approach to the problem of fever of unknown aetiology is not one that concentrates on the elevated temperature alone but one that involves a through search for its cause. The patient should not be unnecessarily exposed to chemotherapy in the hope, often in vain, that, if one agent is not effective, another one or a combination of antibiotics will be helpful[26].

Sub-therapeutic dosage and duration

Successful therapy with antimicrobials depends upon achieving antibacterial activity at the site of infection for a duration long enough to irreversibly overcome the

pathogen. If the drug is not administered in enough dosage to achieve this concentration at the site of infection and/or if the treatment is not continued for a specific period of time, therapeutic failure is quite likely.

The sub-therapeutic use of antibiotics is usually a consequence of one (or more) of the following reasons:

1. In private practice setups where the physician, in addition to seeing the patient, dispenses medication as well, the amount of medicine dispensed is usually just for a couple of days. Similarly, in hospital pharmacies, the amount of medicine provided to patients is maximum of a three days dose[27]. In both the instances, the dose of an antibiotic is almost always sub-therapeutic.

2. Even when patients are clearly instructed to complete a "course" of the prescribed antibiotic, they are likely to discontinue it as soon as their symptoms abate.

3. When prescribing antibiotics that are viewed as "toxic", e.g., chloramphenicol, gentamicin etc., physician is likely to prescribe it in a low-dose and short duration, resulting in sub-therapeutic administration of the drug.

Overuse of antibiotics

The excessive use of drugs, particularly antibiotics, is one of the major problems of present day medical practice[28]. In addition to their use in viral infections a fevers of non-bacterial origin, antimicrobials are overused in other instances as well. These include:

1. It is not uncommon to see patients receiving antibiotics for a duration well beyond what is recommended for chronic infections like tuberculosis.

2. Overuse of antimicrobials is also common in patients who have some noninfectious chronic illness that predispose the individual to infection. For example, it is not unusual to see patients of benign hypertrophy of prostate and chronic obstructive pulmonary disease receiving antibiotics merely because of their vulnerability to infection.

3. Antimicrobials are used for chemoprophylaxis extensively and unnecessarily (see below).

4. As discussed above, antimicrobials are overused in the form of inappropriate combinations with a hope to eliminate the infection rapidly.

5. Since both manufacturers and prescribers give too much encouragement to the indiscriminate use of antibiotics, it is hardly surprising that ordinary people have come to see antibiotics as panaceas. In developing countries, overuse and inappropriate use of antibiotics also results from self-medication by the patients because of their over-the-counter availability[22,29].

Use of "potent" antibiotics

Potent broad spectrum antibiotics initially directed towards hospital use, for example, the quinolones, are now available in oral form and are being promoted for use in the community[20]. Their unrestricted availability has made the physicians' job of treating infections easy, which they can now do without exerting themselves to establish a diagnosis. An unfortunate consequence is that these antibiotics are excessively and inappropriately used to treat conditions that can be effectively cured by one of the older antimicrobials.

Antimicrobial Chemoprophylaxis

Antimicrobial chemoprophylaxis means administration of drug/s to prevent the acquisition and establishment of pathogenic microorganisms. In a broader sense, it also includes the use of drugs soon after colonization by or inoculation of pathogenic microorganisms but before the development of disease.

In practice, antimicrobial chemoprophylaxis is used for a wide variety of reasons. It is specially common in hospitals, where according to several surveys, 30-60% of antibiotic use is for prophylaxis[30]. Despite the widespread administration of antibiotics to prevent infection, their use in this way remains controversial and their value often unproven. Yet chemoprophylaxis is practiced so extensively that it has been pointed out to "account for some of the most flagrant misuses of these drugs[31]".

Some general principles that can be of help for rational use of antimicrobials for chemoprophylactic purposes are[31,32,33]:

1. In all proposed uses of prophylactic antimicrobials, the risk of the patient's acquiring an infection must be weighed against the toxicity, inconvenience, cost, and enhanced risk of superinfection resulting from "prophylactic" drug. It should be used only in situations where its efficacy has been documented.

2. Prophylaxis should be directed against a specific pathogen or defined group of pathogens or used to prevent infection at a specific site. An effort to prevent all types of microorganisms in the environment from establishing themselves only selects the most drug-resistant organisms as the cause of a resulting infection.

3. The shorter the duration of prophylaxis, the broader the range of pathogens that may be prevented. Thus, prevention of "all" infections in severely leukopenic patients by broad-spectrum antimicrobial prophylaxis is successful only over the short-term (resistance developing with long term-usage), whereas lifetime prophylaxis against group A streptococci infections is possible.

4. Prophylaxis is more effective against the pathogens that are poorly able to develop resistance to the drug used.

5. Prophylactic administration of antimicrobials generally requires doses equal to those used for therapy.

6. Drugs effective for therapy may be relatively ineffective for prophylaxis and vice versa. For example, penicillin is highly effective treatment for meningococcal disease but is clinically ineffective for prophylaxis, because it does not eliminate colonization of the nasopharynx. Rifampicin, highly effective for prophylaxis of meningococcal disease, is not recommended for therapy.

7. In clean elective surgical procedures (i.e., procedures during which no tissue bearing normal flora is traversed, other than the prepared skin), the disadvantages of "routine" antibiotic prophylaxis generally outweigh the possible benefits.

8. In surgical procedures, prophylactic administration of antibiotics should generally be considered only if the expected rate of infectious complications approaches or exceeds 5%. (An exception to this rule is the elective insertion of prostheses, where an infection could have catastrophic effects).

9. Prophylaxis for surgical procedures should be started immediately (not more than 2 hours) before surgery and should not be continued for more than 12-48 hours after surgery. Prolonged administration of the antimicrobial drug tends to alter the normal flora of organ systems, suppressing the susceptible microorganisms and favoring the implantation of drug-resistant ones. Exceptions include procedures that involve implantation of a foreign body, in which case antibiotics are often continued until all drains are removed.

10. To achieve chemoprophylaxis in surgical procedures it is not necessary to employ one of the latest broad-spectrum antibiotics. In fact, it should be non-toxic and inexpensive and should not be essential for therapy of serious infections. (Many second- and third-generation cephalosporins are promoted for single-dose surgical prophylaxis. There is no data proving that these agents are more effective than a single dose of cefazolin).

Antimicrobial Resistance - The Cost Of Their Misuse

Any newly discovered or developed antimicrobial has a naturally defined spectrum of "sensitivity" and "resistance". That is, certain microorganisms are sensitive to its antimicrobial effect while others are able to resist the effect. Unfortunately, with its continued use this spectrum of activity can subsequently change to a remarkable degree and microorganisms previously sensitive to the drug can become resistant to it by an array of ingenious alterations. The drug is then no more effective to halt the growth of those specific microorganisms at maximum concentrations that can be tolerated by the host.

The process of development of antimicrobial resistance is directly related to the way it is used. Though resistant strains can emerge even when an antimicrobial is appropriately used, the probability of getting such strains increases manyfold if it is used inappropriately and unnecessarily. This problem of development of antimicrobial resistance, specially when it is misused has been identified since the discovery of first antibiotic. Alexander Fleming, who discovered Penicillin, warned in a 1945 interview by The New York Times that misuse of the drug can lead to the selection and propagation of mutant forms of bacteria resistant to the drug. He warned the medical world that:

> *"the greatest possibility of evil in self-medication is the use of too small doses so that instead of clearing up infections, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed to other individuals and from them to others until they reach someone who gets a septicemia or pneumonia which penicillin cannot save*[34]*."*.

Some bacteria are naturally resistant to certain antibiotics, but often resistance is acquired. Because of antimicrobial resistance, many microorganisms that were effectively being tackled by antimicrobials are again emerging as a potential threat to humans. Multi-resistant strains of organisms associated with "common" infections, like N.Shigella, H.influenzae, E. coli, and S. aureus have been reported from throughout the world. Infections caused by these and other resistant organisms are of much concern because they are likely to cause treatment failure, prolonged illness, frequent and prolonged hospitalization, increased costs, and a higher death rate[7,35,36].

Antimicrobial resistance is not constrained by local or even national borders. Resistant organisms arising from one individual can spread to other individuals, other localities, and consequently to other countries. The problem confronts all individuals and populations around the world and, therefore, is of global concern. Inappropriate, excessive, unnecessary, and sub-therapeutic use of antimicrobials significantly contribute to this problem[23,29,37]. To ensure that physicians contribute minimally to this problem specific to use of antimicrobials, both for the sake of patient and community at large, they should always refrain from inappropriate and irrational use of antimicrobials.

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Chapter 11

Psychotropics - Not A Solution To Every Problem

Psychotropics are drugs used to treat mental disorders. In 1950s, when few of such drugs were discovered, they were called tranquilizers because of their sedating and calmness-inducing effects. They were grouped into major tranquilizers - drugs that calmed down patients of "major" psychiatric disorders like schizophrenia and mania, and minor tranquilizers - drugs that were effective in sedating patients of "minor" psychiatric disorders such as anxiety and depression. Over the last couple of decades, with a better understanding and categorization of mental disorders and discovery of multitude of newer psychotropics, it has been appreciated that the term tranquillizer, as well as major and minor psychiatric disorders, are vague and misleading and now, for scientific reasons, their use is best avoided. Currently, based primarily on their clinical utility, psychotropics are grouped into four categories namely: antidepressants, antianxiety-hypnotics, antipsychotics, and mood stabilizing agents. Each of these major category is further divided into sub-groups, in most instances according to their basic chemical structure. This chapter provides a review of some applied aspects of use of psychotropics and focuses on the commonly observed patterns of their irrational use (mood stabilizing agents, however, have not been discussed because they are very rarely used by nonpsychiatrists).

Factors contributing to the irrational use of psychotropics

Psychotropics, specially benzodiazipines, are among the most misused group of drugs. They are used indiscriminately, are suggested for conditions for which they are not indicated, they are given in inappropriate dosage and for a duration that is inappropriately short or unnecessarily long, and they are prescribed in irrational combinations. Reasons particularly contributing to their misuse are:

1. Training in psychiatry is not given much significance in the medical schools, specially of the developing countries. Psychiatry is just taught as one of the sub-specialities of general medicine and students are given a few weeks, or a couple of months of clinical training in the speciality. Not infrequently, students attend to this training reluctantly because, in the absence of any compulsory component in the examination curricula, students can manage to get through their

examinations even without having any idea about mental disorders and their management.

2. After graduation, physicians who have little knowledge about the psychiatric illnesses and phenomenon, because of the extremely limited training they had received in the medical school years, are generally not much hesitant in prescribing psychotropics. While many physicians do not have much information about the preparations of the specialities they are not practising, say for example, dermatology, paediatrics, gynaecology etc., and consequently avoid prescribing those preparations, many of them somehow get familiar with various psychotropic preparations and prescribe them inconsiderately (salesmen of the psychotropic manufacturers are an important source of making physicians familiar with the psychotropic preparations, who, invariably, visit most of the physicians irrespective of the doctors' speciality).

3. Accurate diagnosis is a prerequisite to the selection and effective use of drugs. In the absence of demonstrable pathological changes, diagnosis of most psychiatric illnesses is a difficult task. It depends upon the objective evaluation of the patient, is almost completely based on inference, and requires theoretical and practical knowledge. Physicians who have not received any formal training in the speciality are, therefore, quite likely to be unable to make a correct diagnosis and, consequently, appropriate therapeutic interventions.

4. Anxiolytic drugs (and a couple of antidepressant-antipsychotic fixed dose preparations) are widely promoted by the manufacturers as a solution to all sorts of worries and stresses, and are portrayed to be of benefit in various physical illnesses. Physicians, majority of whom uncritically rely upon the information provided by the manufacturers, get influenced by such promotional claims of the industry and prescribe these drugs extensively for conditions for which they are, in fact, not recommended.

Antipsychotics

Antipsychotic drugs are also known as "neuroleptics" and (misleadingly) as "major tranquillizer"[1]. They are used for the treatment for psychotic illnesses, that are primarily characterised by disturbance in mood, perception, thought, and behaviour. They are most appropriately used in the treatment of schizophrenias, brief psychotic conditions, mania in the course of bipolar mood disorder, and, more rarely, depression accompanied by psychotic features. In the short-term, they are also employed to quieten disturbed patients of organic psychotic disorders that may result, for example, from brain damage, or toxic delirium. Their use beyond these indications, in most instances, does not have any scientific justification and is irrational. Table 1 enlists the commonly used antipsychotics along with some of their clinically significant characteristics.

Table 1. Commonly used antipsychotics

Drug	Usual oral daily dose (mg)	Relative potency (in mg)	Sedative effects	Extra-pyramidal effects	Hypo-tensive effects
Chlorpromazine	200-800	100	+++	++	++(oral), +++(I.M.)
Thioridazine	150-600	100	+++	+	++
Fluphenazine	2-20	2	+	+++	+
Trifluoperazine	5-20	5	+	+++	+
Haloperidol	2-20-	2	+	+++	+

Note: The potency of drugs (i.e., dose on a weight-for-weight basis) should never be confused with efficacy, as despite greater potency, "low dose" antipsychotic drugs for example, offer no advantage in terms of total efficacy. They do, however, offer a generally higher ratio between the desired and undesired effects.

Antipsychotics cause sedation but are not recommended as "sedatives"

Although some of antipsychotics, for example trifluoperazine, have a clinical reputation of "activating" drugs, they are by no means stimulants[2]. All antipsychotics cause sedation that varies for different antipsychotics (Table 1).

The sleep-producing effects of antipsychotic drugs can be exploited in managing psychotic patients. For patients who are very disturbed, excited, and sleepless, bedtime administration of a sedating antipsychotic will benefit both insomnia and daytime psychiatric symptoms. In others who have a normal or increased sleep use of a less sedating antipsychotic can help avoid unnecessary sedation. However, it should be remembered that the sedative property of a drug is not in itself a suitable basis for choice; it now seems quite clear that adequate doses of drugs with low sedative properties, such as trifluoperazine or haloperidol, may be highly effective for controlling excited or combative patients[3].

Because of the sedative effect of these drugs, some doctors employ them to calm down anxious patients, while others may use them as hypnotics for the management patients who have difficulty with their sleep. Because these drugs are indicated for specific psychiatric conditions and sedation is just one of their side effects, their use primarily for anxiety or insomnia is not recommended[4]. Any such use of these drugs is completely unjustified[5]. Though it might not be as much dangerous, but it is as irrational as prescribing an opiate analgesic, because of its sedating properties, to someone who is just anxious or sleepless.

Extrapyramidal side effects of antipsychotics

All antipsychotics cause extrapyramidal side effects of varying degrees (Table 1). The extrapyramidal side effect of acute onset is acute dystonic reaction, which may appear only after a few doses of the drug or a couple of days after administering a long acting depot-preparation. It is manifested as acute contractions of the muscles of the face and spine, and may be associated with occulogyric crisis. The reaction is distressing, painful, and terrifying, both to the patient and his family members. A relatively longer use of these drugs can result in drug induced parkinsonism which has features of Parkinson's disease, or akathesia which is a state of psychomotor restlessness and is likely to be misinterpreted as a part of the illness. Tardive dyskinesia, another form of extrapyramidal symptom, usually results from long-term use of antipsychotic medication and is characterised by involuntary movements, mainly of the face, extremities, and trunk.

Except tardive dyskinesia, all the extrapyramidal effects of antipsychotics can be managed by discontinuing the medication and by administering anticholinergic drugs. Benzodiazepines may be of additional help in controlling the restlessness associated with akathesia. Tardive dyskinesia usually does not remit even after discontinuation of the therapy and does not have any established treatment. Because it results from long-term use of antipsychotics, unnecessary use of these drugs for long durations should always be avoided.

All the extrapyramidal side effects of antipsychotic drugs are very troublesome and distressing to the patient and, indirectly, to his family members. Any physician who prescribes antipsychotics should be aware of the possibility of these side effects, should be able to identify them when they appear, and should be capable of making appropriate interventions to prevent or manage them. Tardive dyskinesia, because it appears only after long-term therapy, is not "anticipated" and taken into account by many prescribers. It needs to be reemphasized here that it is an irreversible, extremely distressing side effect of antipsychotics which, in many instances, can be prevented by limiting the use of these drugs only for situations where they are really indicated.

Use of anticholinergic drugs to prevent extrapyramidal side effects

The extrapyramidal side effects resulting from short-term use of antipsychotics can be prevented by concomitant use of anticholinergic drugs like procyclidine. Though literature from the developing countries recommends that anticholinergic drugs should be started only after the appearance of an adverse extrapyramidal effect of antipsychotics[1,6], mainly because such an effect is not predictable and does not occur in all the patients receiving an antipsychotic, the approach does not seem to be feasible to be practised as a routine in the developing countries. However, as the anticholinergic drugs have side effects of their own, that may specially become prominent and troublesome if the patient is an elderly or if the prescribed antipsychotic also has prominent anticholinergic side-effects, an attempt always

should be made to keep the dose of the anticholinergic drug the lowest possible. In situations where the extrapyramidal side effects can be recognised or reported by the patient as soon as they appear, for example, when the patient is under indoor care, the anticholinergic therapy preferably should be started after the appearance of these effects.

While it appears that many physicians are aware of the fact that anticholinergic drugs can be used to prevent the extrapyramidal effects of antipsychotics, it, at the same time, seems that many of them are not skilful enough to adjust the dose of the anticholinergic in accordance with the dose of suggested antipsychotic. Not infrequently, patients receiving an antipsychotic that has a minimal potential of producing extrapyramidal side effects are seen receiving high doses of anticholinergic drugs. Contrarily, those on antipsychotics well known for their extrapyramidal side effects might be found using the anticholinergic in a sub-optimal dose and may present with one of the extrapyramidal side effects. To prevent the extrapyramidal effects of antipsychotics and, at the same time, to use the anticholinergic drugs in the best possible way, physicians prescribing antipsychotics should be aware of the extrapyramidal effects-producing potential of various antipsychotics, and be capable of adjusting the dose of anticholinergic drug according to the clinical requirements.

Antidepressants

Antidepressants are used to treat depression (Table 2). Depression here refers to a specific clinical entity that has specific symptoms and "signs". Generally, it is significantly different from the term "depression" as employed by laymen or conceived by some physicians - it is distinct from normal grief, sadness and disappointment, and dysphoria and demoralization often associated with medical illness.

Table 2. Commonly used antidepressants

Drug	Usual oral daily dose(mg)	Sedative effects	Anticholinergic effects
Amitryptaline	50-150	+++	+++
Imipramine	50-150	++	++
Clomipramine	75-150	++	++
Dotheipin	75-150	++	++
Meprotiline	75-150	++	+
Mianserin	30-90	++	0/+
Trazodone	150-200	++	0/+
Fluoxetine	20-40	0	0
Fluvoxamine	50-200	0	0

Antidepressants are viewed by many prescribers that cure depression. This far it is correct but what depression is and for what specific depressive states antidepressants are indicated for may not be within the professional grasp of many of them. They may have a misconception that antidepressants are of help to any patient who is worried, sad, and "depressed" (as a patient himself might report). It needs to be appreciated that antidepressants are indicated for depression as an illness, which like hypertension, diabetes mellitus, asthma, appendicitis, or for that matter any other medically defined illness, has specific clinical features and diagnostic criteria. If a physician is really keen to prescribe antidepressants, it is his professional and ethical obligation first to be familiar with basic concepts of psychiatric illnesses. Prescribing antidepressants, merely because a patient feels sad or reports himself to be "depressed" may be inappropriate on many instances. It would amount to be prescribing antihypertensives to a patient who presents with a complaint, "my blood pressure remains high" without checking his blood pressure, or performing a laparotomy on a patient who presents with a preconceived diagnosis of cholelithiasis without confirming the diagnosis, and the need for the operation.

Of further concern is that many a time physicians may not suggest antidepressants when they are in fact needed. It has been shown that, even in developed countries, as many as half of the depressive illnesses are not recognized as such by primary care physicians. The diagnosis is particularly likely to be missed when the presenting symptoms are more physical than psychological complaints, or when there is a dual diagnosis, with depression accompanying a physical illness[7].

Dose and duration of treatment with standard antidepressants

The standard (tricyclic) antidepressants, if given in recommended dosage, take about two weeks before their antidepressant effects start getting evident. In some patients it may take even longer than this to see the results; more than one quarter of the patients in controlled trials of several antidepressant drugs have improvement only after four weeks of treatment[8]. Therefore, a full trial of a tricyclic antidepressant drug to determine response must involve an adequate dose and duration of treatment.

With a lifetime morbid risk of between 5 and 10%, depression is one of the most common of major mental disorders. But the condition is underdiagnosed and undertreated[9]. Not infrequently, physicians prescribe antidepressants in subtherapeutic doses. Reasons for such a "guarded" therapeutic intervention seem to lie in deficient knowledge about psychotropics and lack of experience with these drugs. Subtherapeutic dose of antidepressants offer nothing but anticholinergic side-effects and some sedation to the patient. Prescribing antidepressants in subtherapeutic dosage results in prolongation of patients' suffering, their unnecessary exposure to troublesome anticholinergic side effects and gradual loss of faith in the treatment, and waste of their money. For effective management of a depressed patient, the prescribing physician therefore should know the recommended dose of antidepressant he is prescribing, and he should wait for a period long enough to let the drug be effective to see the therapeutic results.

Another important consideration, while treating a patient with antidepressants, is to when to stop the drug. While it is recommended by the World Health Organization that antidepressants should be continued in full doses for at least 6 months after full remission of depressive illness[10], many clinicians are of the view that it should be maintained for 12 months[8]. As relapse rates are much higher if treatment is discontinued earlier[7], the prescribing physician should not tapper off the antidepressant for at least six months after complete remission of the illness. Furthermore, as the patient is likely to discontinue the treatment because of his "feeling" that he has recovered, physicians should communicate to the patient about the adverse outcome of an early discontinuation of the treatment, and make efforts that he complies to it.

Informing the patient about the side effects and reassuring about recovery

All the conventional tricyclic antidepressants have predictable anticholinergic side effects. These include dryness of mouth and other mucosal membranes, visual blurring and difficulty in accommodation, constipation, a variable degree of difficulty in passing urine, and tachycardia and dizziness. Because of these anticholinergic effects, tricyclic antidepressants are not recommended for use in patients having some cardiac disease, glaucoma, or benign hypertrophy of prostate. All the anticholinergic effects are discomforting to the patient and, unlike the therapeutically desired effects of the drug, they appear as soon as the medicine is started. Because of the uneasiness and discomfort associated with these effects, and in the absence of any obvious improvement in the clinical condition, patients are likely to stop taking the drug if they have not been counselled prior to the initiation of the treatment. Reassurance at the start of treatment is vital to ensure patient's compliance to the treatment. In addition, as the desired therapeutic effects start appearing after a couple of weeks of initiating the therapy, depressed patients should also be told that they will improve, but that there may be several weeks before this becomes apparent[11].

The anticholinergic side effects, though somewhat discomforting for the patient, are as such of not much medical concern for otherwise physically healthy patients. These patients should be encouraged to persist with the treatment. Because some tolerance to these side effects seems to develop, and as the patient will start feeling improvement in his mental condition, the side effects would not remain significantly troublesome for him. These effects can be reduced if low doses of antidepressant are given initially and then gradually increased, but this must be balanced against the need to obtain adequate plasma concentrations as soon as possible.

Antidepressants are not recommended for use as sedatives

Antidepressants (the tricyclic and the related ones) cause varying degrees of sedation. Some are less sedating than others but none of them is a "stimulant". The

difference in the sedative effect of different antidepressants may be pertinent to making their choice; a patient who is agitated and restless can be given one of the more sedating antidepressant, while for a patient who is withdrawn a less sedating one will be more suitable. It, however, should be born in mind that the sedating potential of antidepressants apparently is unrelated to their clinical efficacy[12].

Because of their sedating effect, antidepressants are prescribed by some physicians as anxiolytics or hypnotics. While in some situations their use for these purposes might be justified, their routine use in this regard is not recommended. Instead, one of the benzodiazepine should be used as an anxiolytic or hypnotic. They have an established clinical utility in this regard and do not possess anticholinergic side effects inherent in most of sedating antidepressants.

Serotonin-selective-reuptake-inhibitor antidepressants

The serotonin-selective-reuptake-inhibitor(SSRI) antidepressants constitute the new generation of antibiotics. As their name suggests, these act as antidepressants by selectively blocking the reuptake of serotonin in the neuronal synapses. Of the SSRIs, fluoxetine has become one of the well-known antidepressant throughout the world. Its "popularity" among physicians is evident from the extent of its consumption - according to an estimation, millions of people have been treated with fluoxetine worldwide and in 1992, just four years after its discovery, fluoxetine had a global sale of $1 billion and was among the top 15 drugs according to sales[13].

The "credit" of such an extensive use of fluoxetine goes to the manufacturers who set forth an aggressive campaign for its promotion as a novel antidepressant. The compound has achieved such a market within few years of its discovery that now numerous preparations of it are available in the market. Contrary to the "impression" of many prescribers, the drug, like other SSRI antidepressants is not superior to many of the conventional tricyclic antidepressants. In an analysis of comparative studies, fluoxetine was not found to be better than imipramine, amitryptaline or dothiepin. However, the dropout rate was higher with the tricyclic antidepressants, specially amitryptaline, because of their troublesome side effects[14]. Though the SSRIs have been found to be effective for mild depression, in general, these newer antidepressant drugs are second-line treatment for patients with severe depression. They may be indicated as initial therapy under special circumstances, such as known intolerance to a tricyclic agent or the presence of a physical illness likely to be adversely affected by the tricyclics[8].

The SSRI antidepressants are promoted as safer alternative to conventional antidepressants but they are not all that safe. Fluoxetine, for example, can cause nervousness, tremors, anxiety, insomnia, nausea, anorexia and weight loss, sexual dysfunction, mania, paranoid or psychotic reaction, suicidal feelings, extrapyramidal symptoms, serum sickness, and syndrome of inappropriate secretion of antidiuretic hormone. It can also cause dangerous interactions with other psychotropic drugs specially tricyclic antidepressants[13,14]. Physicians who believe that SSRIs are "very

safe" and "very effective" antidepressants, and prescribe them without much constrain should, therefore, better be at a lookout when suggesting one of these compounds to a patient.

Anxiolytics/Hypnotics

Anxiolytic drugs, also called sedatives, are used to relieve a patient of his anxiety. These drugs decrease activity, moderate excitement, and calm the recipient. Hypnotic drugs produce drowsiness and facilitate the onset and maintenance of sleep. Most of the currently available sedatives are also hypnotics when used in relatively higher doses.

The first agent to be specifically used as sedative and soon thereafter as hypnotic was bromide, in early part of second half of nineteenth century. Four more sedative-hypnotic drugs, namely chloral hydrate, paraldehyde, urethane, and sulfonal, were in use before 1900. With the discovery of barbital in 1903 and phenobarbital in 1912, barbiturates took over the market of sedative-hypnotics. But with the introduction of chlordiazepoxide in 1961 the era of benzodiazepines began. Since then, more than 3000 benzodiazepines have been synthesized, over 120 have been tested for biological activity, and about 35 are in clinical use in various parts of the world[15].

The real differences among different benzodiazepines

The pharmacokinetic, physicochemical, and pharmacodynamic properties of benzodiazepines differ, yet current evidence suggests the therapeutic response to these drugs is broadly similar. There is little to choose among the benzodiazepines in terms of either safety or efficacy. "As far as any real distinctions between the differently labelled pills are concerned, they are as subtle as those between a brick and a half brick[16]". While some benzodiazepines are advertised with an emphasis on their anxiolytic effect and others are promoted as hypnotics, the differences between them are subtle and possibly insignificant in some cases[17]. Claims of particular advantages for individual drugs have encouraged prescribers to reserve certain preparations for specific indications, a policy which often results in patients receiving more than one pharmacologically similar entity. It is unlikely that this represents optimal practice, since it may facilitate toxicity, is inconvenient to the patient and is expensive[18].

The difference between various benzodiazepines that is of significance while making a therapeutic choice is their plasma half life. Benzodiazepines that have an intermediate to long half-life provide a relatively sustained "sedative" effect than those having short half-life and generally are more suitable as anxiolytics. Contrarily, benzodiazepines with short half-lives are less likely to have a daytime hangover effect and, in general, are more suitable as hypnotics. Because many of the benzodiazepines have active metabolites, that can sustain their sedative effect, the presence (or

absence) of active metabolites of benzodiazepine being prescribed also has to be taken into consideration.

This alone, however, is not a criteria for the selection of a benzodiazepine for any particular patient. In choosing the appropriate benzodiazipine, clinicians also should take into account the patient's age and medical status, the anticipated duration of treatment, the specific blend of symptoms and special needs, and the pharmacologic spectrum desired[4].

Differences between benzodiazepines of short and long half-life

Pharmacological characteristics of benzodiazipines, that are of clinical significance, are largely dependent upon the half-life of the benzodiazipine being prescribed. To prescribe benzodiazepines in a rational way, physicians, therefore, should be aware of the half-lives of various benzodiazepines (Table 3), and know how benzodiazepines of different half-lives differ from each other. The clinically significant differences are summarized in Table 4 and are briefly discussed below.

1. Generally, benzodiazepines that do not have active metabolites, like lorazepam, temazepam, and triazolam, have shorter half-lives as compared to those having active metabolites, like diazepam, chlordiazepoxide, and chlorazepate.

2. In contrast with the benzodiazipines of long half-lives, that get accumulated in the body and have a long lasting sedative and hangover effect, benzodiazepines of short half-life are excreted rapidly from the body and do not cause such effects. However these may cause early morning insomnia and daytime rebound nervousness[19].

3. Benzodiazepines with intermediate to long half-lives, because of their sustained sedative effect, are preferably used as anxiolytics. Those with short half-lives are generally used as hypnotics.

4. Benzodiazepines with long half-lives are as good as hypnotics as the short acting benzodiazepines, provided they are used in correct dosage. If a patient who is receiving a long acting benzodiazepine for his anxiety develops insomnia, there is no rationale in prescribing him another benzodiazepine that is "viewed" to be a hypnotic. Instead, an increase in the bedtime dose of the benzodiazepine he already is taking will not only improve his sleep, it will also offer him control over his daytime anxiety.

5. Short acting benzodiazepines do not get accumulated in the body and their effects are more predictable than the long acting ones. That is why they are preferred for use in the elderly[20].

6. Abrupt discontinuation of benzodiazepines with short half-lives, as opposed to those with long half-lives, is associated with an increased likelihood of

discontinuation syndromes and are difficult to discontinue. It may be particularly difficult for patients to discontinue alprazolam[4], which seems to be a favourite "all-purpose" medication for many physicians. Benzodiazipines with short half-lives should therefore be used for very short durations and stopped gradually rather than abruptly[21].

7. Anterograde amnesia has been reported with most benzodiazepines. The risk may be higher with short-acting varieties, such as lorazepam and triazolam[4] and has to be taken into consideration when prescribing these to patients of old age, who already might have some cognitive deficit.

Table 3. Metabolites and half-lives of commonly used benzodiazepines

Drug	Metabolites	Half-life(hours)
Alprazolam	Inactive	10-15
Bromazepam	Active	8-19
Chlordiazepoxide	Active	5-30
Chlorazepate	Active	50-100
Clobazam	Active	32-50
Diazepam	Active	50-150
Lorazepam	Inactive	10-18
Lormetazepam	Largely inactive	9-15
Nitrazepam	Probably inactive	24-36
Temazepam	Possibly active	5-8
Triazolam	Active	3-5

Adapted from: Trevor AJ, Way WL. Sedative-hypnotics. In: Katzung BG (ed.). Basic and clinical pharmacology. USA; Appleton & Lange, Connecticut, 1989. p268. And, Hollister LE. Psychiatric disorders. In: Speight TM (ed.). Avery's drug treatment - Principles and practice of clinical pharmacology and therapeutics (3rd ed.). Scotland: Edinburgh, ADIS Press Ltd. 1987. p1146-47.

Table 4. Comparison of short-acting and long-acting benzodiazepines

Characteristic	Short acting	Long acting
Accumulation with repeated use	No	Marked
Hangover effects next day, sedation	Mild	Moderate
Tolerance	Moderate	Mild
Anterograde amnesia	Moderate	Mild
Risk of rebound insomnia	Moderate	No
Risk of daytime anxiety	Mild	No
Anxiolytic effect next day	No	Moderate
Full benefits on first night	Moderate	Moderate

Reproduced from: Gillin JC, Byerley WF. The diagnosis and management of insomnia. In: Oates JA (ed.), Wood AJJ (Assoc. ed.). Drug therapy. N Engl J Med. 1990;322:239-248.

Suggested duration of treatment with benzodiazepines

Benzodiazepines are far from safe. All benzodiazepines, in addition to causing the well known side effects like drowsiness, anterograde amnesia, and some difficulty in motor coordination, carry a potential risk of inducing psychological and physical dependence. Chances of developing dependence are greater with the use of short-acting benzodiazepines as compared to the long-acting ones, but it needs to be kept in mind that none of them is safe for long-term use. It has been estimated that between 15 and 44% of long-term users of benzodiazepines become dependent on the drugs[16]. Therefore, it is prudent not to use these agents indiscriminately to treat minor and situational anxiety. Both the Committee on Safety of Medicines and the Royal College of Psychiatrists advise that benzodiazepines are indicated only for short-term relief of anxiety that is severe, disabling or causing a patient unacceptable distress. They also have stipulated that continuous benzodiazepine therapy should rarely extend beyond one month[22].

Further, benzodiazepines should not be used for longer periods because with continuous use their anxiolytic effect wanes off, because of the development of tolerance to these drugs. The Committee on Review of Medicines(UK) has advised against using benzodiazepines in long-term management of anxiety because of lack of evidence that their efficacy as anxiolytics extended beyond four months. It recommends that benzodiazipine therapy should be short-term, carefully monitored and withdrawn gradually to minimize withdrawal symptoms[22].

Use of benzodiazepines as hypnotics

The short acting benzodiazepines, when used in appropriate doses, are very effective hypnotics and are widely used for this purpose. Three important therapeutic facts that need to be taken into account when using these agents as hypnotics are:

1. Frequent or prolonged use of benzodiazepine hypnotics can disturb the patient's normal sleep pattern. In particular, benzodiazepines with very short half-lives can cause early morning insomnia and daytime nervousness, giving the patient a "tired and sick" feeling.

2. A hypnotic may be given with a belief that improved sleep will improve daytime performance. But numerous studies have shown dose-dependent impairment rather than improvement of performance during the administration of hypnotic drugs[4].

3. Benzodiazepines can cause dependence even when they are used as hypnotics[23]. Long-term treatment with hypnotics is, therefore, not recommended[4].

Non-psychiatric reasons of benzodiazepine use

Psychotropics are used extensively for nonpsychiatric conditions and are frequently prescribed by nonpsychiatrists. Surveys in some countries have concluded that nonpsychiatric physicians, specially the general practitioners, prescribe the majority of psychotropic medications[23,24,25]. Of the psychotropics, sedative/hypnotics and antidepressants are the most commonly prescribed groups of psychotropics in nonpsychiatric settings[26]. Such an extensive use of psychotropics (benzodiazepines) stems form:

Psychiatric disorders have somatic symptoms

Many psychiatric disorders have prominent somatic symptoms. This is specially true for depressive illness and generalized anxiety disorder. For example, it is estimated that approximately 50% of patients with generalized anxiety disorder have predominantly somatic distress referable to cardiovascular system, gastrointestinal tract, or other organ systems. Many of these patients consult a nonpsychiatrist, undergo evaluation for physical disease, and are prescribed some psychotropic when no physical abnormality is identified[21].

Benzodiazepines are frequently suggested for physical illnesses

Benzodiazepines and antidepressants are frequently prescribed by nonpsychiatrists as an adjuvant to treatment of various physical illnesses. In a survey, the prevalence of psychotropic drug use in outpatient medical settings generally ranged from 10-15%[25]. Another study found that up to 40% of patients who are first prescribed a psychotropic drug (usually an anxiolytic) present with a physical complaint and 20% of patients may become chronic users[27]. The nonpsychiatric conditions for which benzodiazepines are frequently suggested include: hypertension, different types of headaches, gastritis and peptic ulcer, and various musculoskeletal conditions. Use of benzodiazepines may not be justified in many of these situations. For example, benzodiazepines are frequently prescribed to patients of muscle spasm following non-serious injury or chronic minor back pain but their efficacy in these conditions is not well supported by clinical studies. Furthermore, at the dose given by most doctors, it is unlikely that sufficient drug concentration at brain stem level, necessary for the clinically important, objective relaxation of peripheral skeletal musculature, would be achieved[27].

Benzodiazepines are prescribed when symptoms are vague

Medical school training tends to focus on the diagnosis and treatment of disease states. When the physician graduates to the world of clinical practice, however, patients may present with complaints related to known disease states less frequently than with complaints of tension, insomnia, headaches, depressive symptoms, anxiety and the like which reflect life stress and are not part of any known disease. The most fundamental decision with regard to anxiety and/or vague somatic complaints

diagnosed as expressions of stress rather than of disease states, is whether to prescribe drugs or to adopt some other means of responding to the stresses concerned. Lack of training in how to respond to such complaints may result in poor prescribing practices and many physicians make their way out of the situation by prescribing psychotropics, usually benzodiazepines, to such patients.

Benzodiazepines are not a solution to everyday stresses

Not infrequently, physicians consider Benzodiazepines (and low doses of antidepressants) are considered by some physicians to be the "drug of choice" for all sorts of stresses and problems. In fact, it is amazing to see the variety of conditions for which benzodiazepines are prescribed: an employee who reports to have a "difficult" boss, a student who is to take his examination within a couple of weeks, a lady who remains tense because of her quarrelsome mother-in-law and troublesome children, a businessman who remains anxious about his investments, a professional who has to compete for his success, or a worried jobless, all are likely to be prescribed a psychotropic (usually a benzodiazepine) if they consult a physician. An important reason for use of benzodiazepines for such "conditions" is that manufacturers portray these agents to be effective and suitable for a wide variety of such situations (Box 1).

Box 1. Benzodiazepines are a solution to every stress!

Benzodiazepines are frequently prescribed for stress, tension, or anxiety that is a consequence of everyday problems that in no way can be solved by using these drugs. An important reason for such an extensive irrational use of these compounds is that they are portrayed by the manufacturers to be useful and effective for persons with such problems. Consider the following example:

"In peru in 1991, a multinational pharma-industry was promoting its alprazolam as a treatment for virtually every condition of daily life. It promised relief for:

- the "syndrome of the modern woman" - who suffers from increased worries about work, and an increased workload, emotional worries and stress;
- the "syndrome of todays man" - who worries about the future, his increased responsibilities, frustrations at not reaching his goals, financial problems and stress;
- the "syndrome of the housewife" - who worries about the children's education, having too much work, financial problems, fear of domestic accidents and a fear of the house being burgled; and
- the "syndrome of the elderly" - who fear being lonely, worry about their health and future, have limited finances, and lack affection.

(Reproduced from: Chetley A/Health Action International. Problem drugs. Health Action International: the Netherlands, Amsterdam. 1993. p190.)

With such a promotion by the manufacturers there is little wonder that benzodiazepines are among the most frequently prescribed medicines worldwide.

It, therefore is an observation that physicians who consider advertising and promotion from pharmaceutical firms to be an important mean of learning about the products prescribe more benzodiazepines[28]. How far these agents can really help individuals with such "complaints" is self evident and does not require any elaboration. It is suffice here to say that benzodiazepines are not prescribable "intoxicant" meant to help a patient to escape the day to day stresses of life.

Prescribing benzodiazepines in old age

The elderly, as a group, are the most likely to be prescribed benzodiazepines[26]. A study estimated that prescribing rates of bezodiazepines increase ten-fold from the age of 20 to 70 years[29]. This higher prescribing rate for the elderly is presumed to be due to the higher prevalence of sleep disturbance in old age. Because benzodiazepines are also suggested as an adjuvant therapy in various physical illnesses, that are more common in the elderly than the younger age group, this might be an additional reason for the higher use of benzodiazepines in this age group.

When prescribing benzodiazepines to the elderly, the following clinical aspects should never be overlooked for safe and rational prescribing of these drugs.

1. The elderly are more sensitive to the CNS depressant effect of these drugs[4,30]. Doses of benzodiazepines, therefore, should be reduced in the elderly. Although there is a trend to prescribe slightly lower doses of some drugs in the elderly, a study found that doses of benzodiazepines were not significantly reduced for the elderly patients, and dose given to some of them were needlessly high[29].

2. Whereas CNS responsiveness to benzodiazepines increases in old age, the cognitive reserve decreases. The elderly, therefore, are more likely to experience cognitive side effects of these drugs, like anterograde amnesia, confusion, and disorientation than the younger patients.

3. The long acting benzodiazepines are specially likely to cause confusion, disorientation, and lack of coordination in the elderly and their long-term use has been associated with falls, hip fractures, daytime sedation, and cognitive dysfunction in the elderly[31].

4. Benzodiazepines that do not have active metabolites, like alprazolam, lorazepam, temazepam, and triazolam are recommended for use in the elderly because their effects are more predictable than those of benzodiazepines with active metabolites[20]. But it should be remembered that the risk of anterograde amnesia is higher with the short-acting benzodiazepines.

Use Of Psychotropics In Combination

Though psychotropics are frequently suggested in combination, there are few situations in which it is scientifically justifiable. The following section provides a brief discussion on the commonly observed patterns of psychotropic combinations, signifying aspects that can help prescribe these agents appropriately and rationally.

Concomitant use of various benzodiazepines

As discussed above, benzodiazepines broadly resemble each other with reference to their therapeutic response. Selection of a benzodiazepine for any particular patient requires consideration of desired onset of effect, duration of action of the drug, age of the patient and the status of his physical health, and a dose and dosage schedule that matches the symptoms of the patient and his needs. Prescribing benzodiazepines in combination is just an unnecessary duplication of the treatment and is irrational.

The short acting benzodiazepines are good hypnotics while the long acting ones are preferably used as anxiolytics. Some physicians view these two therapeutic groups of benzodiazepines as distinct and use them in combination. Because both these effects can be achieved by use of an appropriately selected single benzodiazipine, it is rarely necessary to prescribe on antianxiety drug for the daytime and another drug for sleep at night[24]. As is clearly mentioned by a textbook of pharmacology[32]:

> *"It makes no sense to combine antianxiety drugs with each other. Among such combinations may be an inadvertent one in which one type of drug is used during the day, because it has been most extensively promoted as a daytime sedative, while another is used at night because it has been labelled by advertising as a hypnotic."*

Other physicians use benzodiazepines in combination perhaps with a view that such a combination offers a better cure for anxiety (Prescription 1). There is no good evidence to support the superiority of any such combination over the proper use of a single benzodiazepine, and the practice is clearly unscientific and irrational. According to British National Formulary[33]:

> *"Prescribing of more than one anxiolytic or hypnotic at the same time is not recommended. It may constitute a hazard and there is no evidence that side effects are minimized."*

Combination of tricyclic antidepressants

Some tricyclic antidepressants have a clinical reputation of "stimulants" while others are recognized as sedatives. This clinical categorization of tricyclic antidepressants may lead a physician to prescribe a so called stimulating tricyclic for the daytime use

Name ..... Age ..... Disease ..... Date 15-2-92

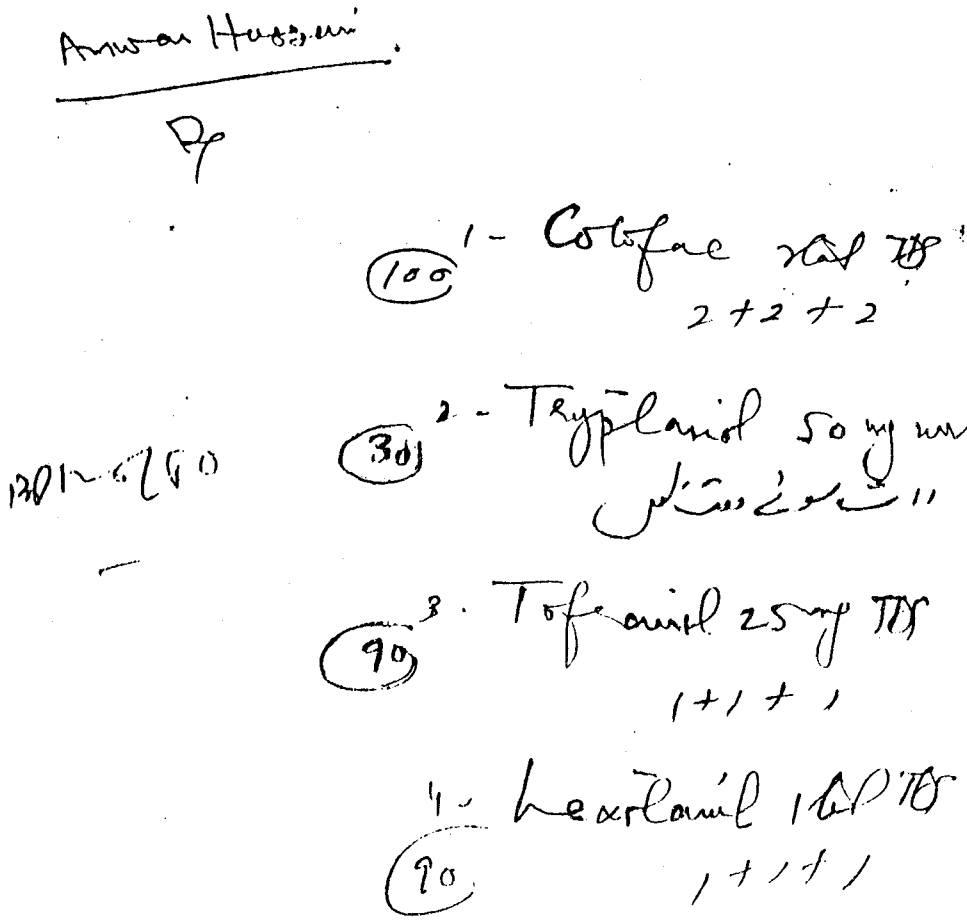
℞ (1) Cap. Tranxene (10mg)
(1) = 10

(2) Tab. Lexotanil (3mg)
(1) = 10

(3) Tab. Frisium
½ = 5

(4) Tab. Duxil
1+1 = 20

PRESCRIPTION 1. An example of unnecessary and irrational combination of benzodiazepines. Tranxene (clorazepate), Lexotanil (bromazepam) and Frisium (clobazam) have been suggested in combination. Appropriate selection of a any one of these, and administration in proper dosage, would had been equally effective and definitely more rational.



PRESCRIPTION 2. Prescribing more than two antidepressants simultaneously does not have any rationale. The prescriber has combined imipramine (Tofranil) with amitryptaline (Tryptanol), perhaps with a belief that the former has "stimulating" characteristics while the later is a sedating antidepressant!

while another one deemed to be having marked sedating properties for use at night (Prescription 2). As a matter of fact, all the tricyclic antidepressants in common use have a sedative effect[8,34] and only protryptyline has some stimulant action[35]. Therefore, any combination of tricyclic antidepressants in this regard is irrational.

Rationale of fixed dose combination products of psychotropics

It is important to mention here that some companies market tablets that contain small amounts of an antidepressant along with a small amount of an antipsychotic. These fixed dose products are promoted by the manufacturers for use in anxiety and depression. These products do not have any scientific rationale for use in either of these conditions and the promotional claims are misleading. The valid indications for such fixed dose preparations are very few and even for these indications they are not deemed suitable[36]. According to a textbook of psychiatry[37]:

> *"Some drug companies market tablets that contain a mixture of drugs, for example, a tricyclic antidepressant with a small dose of phenothiazine. These mixtures have little value. In the few cases when two drugs are really required, it is better to give them separately so that the dose of each can be adjusted independently."*

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Chapter 12

Non-Steroidal Anti-Inflammatory Drugs - Too Many But All The Same

Pain is one of the most common symptoms and one of the most frequent reasons why people seek medical care. It is not surprising, therefore, that analgesics are among the most used categories of drugs[1].

Pain, if unrelieved, is quite incapacitating and has an adverse effect on the quality of life of the patient and his family. Therefore it is important to intervene to treat pain before it becomes severe and disabling. Fortunately, pain, whether due to trauma, surgery, cancer, osteoarthritides, or other diseases can usually be managed effectively through relatively simple means if applied appropriately.

Pain is a physiological response but many emotional and cultural factors influence the perception of pain. The primary cause (e.g, trauma, infection), pathogenesis (e.g., inflammation, ischemia) and contributory factors (e.g., recent changes in life situation, symbolic attributes of pain) must all be sought in management of pain.

In 1992 and 1994, the Agency for Health Care Policy and Research of U.S. Department of Health and Human Services published two clinical practice guidelines for management of Acute Pain and Management of Cancer Pain[2] (Box 1). The AHCPR guidelines emphasize that although pain cannot always be entirely eliminated, appropriate use of drugs and other therapies can effectively relieve pain in majority of patients.

Drugs Used In Pain Management

Drug therapy is fundamental to pain management. When employed properly it is effective, carries little risk and is rapid in onset. Drugs used to treat pain are called analgesics. There is no internationally agreed upon classification of analgesics[3]. Some text books classify them according to their effectiveness in treating either mild or severe pain. Others classify them according to where they work either at the site of the pain or on the brain. Pain relievers that work at the site of pain block the production of prostaglandins, which in term prevents the stimulation of nerve endings so no pain message is sent to the brain; those that work on the brain block the transmission of pain signals between brain cells and therefore interfere with

perception of pain. Another approach is to talk about narcotic or opioid analgesics (those analgesics of natural or synthetic origin with actions like morphine) and non narcotic or non-opioid analgesics (such as aspirin). Narcotic analgesics may produce drug dependence. They are used frequently and effectively to relieve severe pain, usually from internal organs, but also from other parts of the body. Non-opioid analgesics are used to relieve skin, muscle, joint, bone or tooth pains. Still another classification divides pain killers into those that simply relieve pain and fever (antipyretics), and those that relieve pain, fever and help to reduce inflammation. The latter are usually described as non-steroidal anti-inflammatory drugs (NSAIDs) or, because aspirin is the prime NSAID, they are sometimes called aspirin-like drugs.

Drugs that relieve pain due to a single cause or specific pain syndrome only, e.g.,ergotamine (migraine), carbamazepine (neuralgias), glyceryl trinitrate (angina pectoris) are not classified as analgesics[4].

Box 1. Recommended clinical approach to pain management

A.
- Ask about pain regularly.
- Assess pain systematically (quality, description, location, intensity or severity, aggravating and ameliorating factors, cognitive responses).
- Ask about goals for pain control, management preferences.

B.
- Believe the patient and the family in their reports of pain and what relieves it.

C.
- Choose pain control options appropriate to the patient, family, and setting.
- Consider drug type, dosage, route, contraindications, side effects.
- Consider nonpharmacologic adjunctive measures.

D.
- Deliver interventions in a timely, logical, coordinated manner.

E.
- Empower patients and their families.
- Enable patients to control their course to the greatest extent possible.

F.
- Follow up to reassess persistence of pain, change in pain pattern,development of new pain.

Reproduced from McPhee SJ, Schroeder SA. General approach to the patient; health maintenance, & disease prevention; & common symptoms. In: Tierney LM,Jr., McPhee SJ, Papadakis MA. (ed.). Current medical diagnosis & treatment. New Jersey: Appleton & Lange. 35th ed. 1996. p12.

How to use analgesics

Pain control does not essentially require use of analgesics. Simply removing the cause of pain can relieve pain. Where the cause cannot be removed physical therapies (message, immobilization, heat, cold, repositioning, exercise) and psychological

measures (patient education and reassurance, relaxation, biofeedback may significantly relieve pain.

Since pain is not a disease but a symptom, long term relief depends on treatment of the underlying cause. For example, the pain of toothache can be relieved by drugs but can only be cured by appropriate dental treatment. When the underlying disorder is irreversible long term analgesic treatment may be needed[5].

When analgesics are needed, they should be prescribed according to some established guidelines. The World Health Organization recommends a three step hierarchy for use of analgesics[2]:

Step I: Use nonopioid analgesics for mild to moderate pain with or without adjunctive agent.

Step II: If pain persists add an opioid to the nonopioid agent with or without an adjunctive agent.

Step III: If pain still continues increase the opioid potency or dosage while continuing the nonopioid and adjunctive agents.

Non-steroidal Antiinflammatory Drugs (NSAIDs)

Non-steroidal antiinflammatory drugs are among the most widely prescribed group of drugs worldwide[6]. They constitute a group of drugs that basically resemble aspirin and have antiinflammatory, analgesic, antipyretic, and platelet inhibitory actions. Currently available NSAIDs come from a variety of chemical classes (Table 1) that differ pharmacokinetically and to some extent pharmacodynamically.

TableE 1. Chemical classification of NSAIDs.

Chemical Groups	Examples
Carboxylic acids	• Acetylated: Aspirin • Non-acetylated: Choline salicylate, diflunisal, magnesium salicylate, salicylamide, salicylate with magnesium salicylate, salsalate, sodium salicylate
Acetic acids	Diclofenac, indomethacin, tolmetin, sulindac, etodolac
Propionic acids	Ibuprofen, naproxen, fenoprofen, pirprofen, indoprofen, tiaprofenic acid, oxaprozin, ketprofen, fenbufen, flurbiprofen, carprofen, suprofen
Fenamic acids	Flufenamic acid, mefenamic acid, meclofenamic acid, niflumic acid
Enolic acids	Oxyphenbutazone, phenylbutazone, piroxicam, sudoxicam, tinoxicam, isoxicam
Non-acidic compounds	Nabumetone, proquazone, bufexamac

Reproduced from Brooks PM, Day RO. Nonsteroidal antiinflammatory drugs - differences and similarities. In: Oates JA. (ed.). Drug therapy. N Engl J Med. 1991;324:1716-1725.

Some misconceptions exist about NSAIDs that lead to extensive, intemperate, and irrational prescribing of these drugs. Three most important ones are briefly discussed bellow:

Misconception 1
NSAIDs differ significantly in their relative efficacy and side effects

The many comparative trials of NSAIDs have rarely revealed clinically important differences between these agents[7]. Experts everywhere agree that differences in efficacy are relatively slight. Review of 179 clinical trials of NSAIDs in osteoarthritis and more than 400 trials in rheumatoid arthritis have not demonstrated significant differences in efficacy, nor they have provided any basis to rank these drugs according to efficacy[8].

There also does not seem to be significant differences among these drugs, with the exception perhaps of ibuprofen at low doses, in the incidence of major side effects[8]. To date there is no clear evidence differentiating equipotent antiinflammatory doses of one NSAID from another with respect to the risk of serious upper gastrointestinal side effects. Similarly there is general agreement that no NSAID can be prescribed with absolute safety with respect to renal side effects[6,7,9].

The claims of manufacturers regarding the superiority of their NSAID over certain others with respect to its efficacy or safety is simply one of the techniques they employ to compete the market[10]. The data presented by them in their promotional material is just a form of statistical jugglery and is misleading. It is therefore essential not to get carried away by such claims.

Misconception 2
NSAIDs are very safe drugs

NSAIDs have commonly been regarded as safe drugs and that is one of the reasons of there widespread use. But there is a current of mounting experience, reports, and studies that have seriously challenged the safety of these drugs as presently used in the practice of medicine. They are one of the most common cause of adverse reactions reported to drug regulatory authorities in the United Kingdom; gastrointestinal effects being the most common followed by renal damage, skin reaction, blood dyscrasias, headache, and nausea[6].

NSAIDs are associated with gastric erosions, peptic ulcer formation, and perforation, major upper gastrointestinal haemorrhage, and inflammation and change in the permeability of the intestine and lower bowel. Present information based on endoscopic evaluations confirms that one out of five chronic NSAIDs users will have ulcer cater disease[11]. Of further concern is that NSAID gastropathy can be a silent disease and NSAID induced dyspepsia does not predict any particular gastric pathologic effect[7,11]. These drugs not only contribute to ulceration but also mask the pain that would normally lead to its diagnosis[12].

At the 22nd meeting of the Arthritis Advisory Committee of the Food and Drug Administration (FDA) of the United States of America on 16th May 1988, an entire session was devoted to developing new class labelling for these drugs and the risk of gastrointestinal ulcerations, bleeding, and perforation with NSAID therapy[11]. This proposed new wording for the package insert and for patient information emphasizes several points. First, serious and fatal events "can occur at any time" in patients chronically treated with NSAIDs. Second mucosal lesions can occur without being associated with symptoms and thus more serious events can occur without premonitory symptoms. Finally, patients with previous lesions, debilitating diseases, and advanced age appear to be most susceptible to the gastric complications. The NSAIDs therefore need more responsible use.

The other major, potentially serious side effects of NSAIDs are those effecting the kidney. They can cause reversible impairment of glomerular filtration, acute renal failure, edema, interstitial nephritis, papillary necrosis, chronic renal failure, and hyperkalemia. They are particularly likely to decrease glomerular filtration in patients with hypovolumic states due to salt depletion or hypoalbumenemia and in those with preexisting renal impairment due to age, atherosclerosis, hypertensive renal disease, or other intrinsic renal disease. In addition, patients of congestive heart failure, cirrhosis, and renal insufficiency are at risk for an acute ischemic insult to the kidney[13]. Prescribing NSAIDs to such patients, therefore, requires extra care. All NSAIDs (possibly except sulindac), and Indomethacin in particular, can interfere with the pharmacological control of hypertension and cardiac failure in patients receiving beta adrenergic antagonists, diuretics, or angiotensin-converting-enzyme inhibitors because of there pharmacodynamic interaction with these drugs. Care has to be taken when these drugs need are prescribed together.

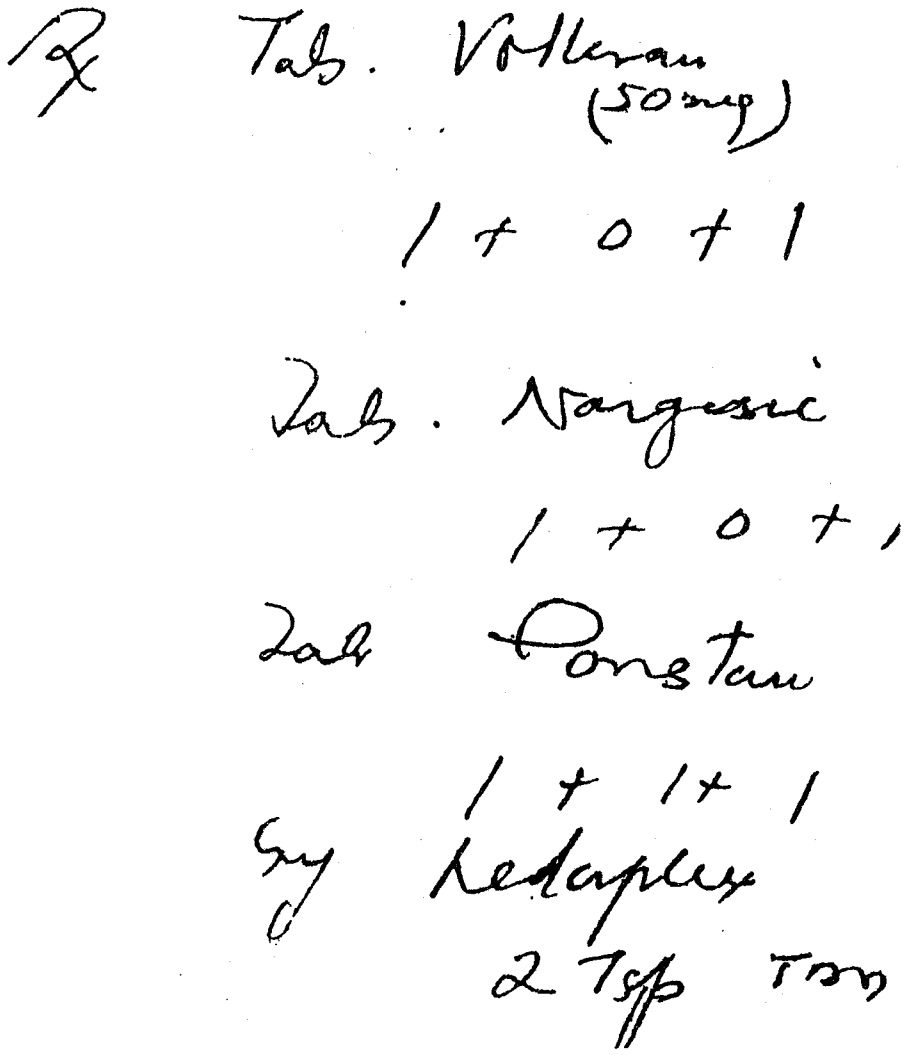
It is important to mention here that Paracetamol, an analgesic that is not an NSAID, is frequently preferred over NSAIDs because of its lesser gastrointestinal side effects. However it carries a greater risk for chronic renal failure[14], specially when it is used in combination with aspirin and is taken jointly with caffeine[15]

Misconception 3
Combination therapy with NSAIDs is more effective

It is not uncommon to see prescriptions containing more than one NSAID (Prescription 1). These prescriptions, if written with a belief that combination therapy with NSAIDs is more effective, are irrational because such a combination usually is not more effective. According to Goodman & Gilman's Pharmacological Basis of Therapeutics:

> *"It is best to avoid continuous combination therapy with more than one aspirin-like drug; there is little evidence of extra benefit to the patient, and the incidence of side effects is generally additive[16]"*

This, however, does not imply that NSAIDs cannot be given in combination. They differ in their pharmacokinetic properties e.g., half-life (Table 2), and relative



PRESCRIPTION 1. More than one NSAIDs are usually prescribed with a belief that such a combination is more effective. In fact, there is little evidence that combination therapy with NSAIDs offers any extra benefit to the patient. Furthermore, when NSAIDs are given in combination, the incidence of their side-effects is generally additive.

antiinflammatory versus analgesic potential (Table 3). They can be given in combination when one of these characteristic is under consideration. According to Laurence's Clinical Pharmacology:

> *"Simultaneous use of two analgesics of different modes of action is rational but two drugs of the same class/mechanism of action are likely to be un-profitable unless there is a difference in emphasis, analgesia versus antiinflammatory action; or a patient taking a NSAID with a long half life e.g. naproxin (14 h), is benefited by having available an additional drug of shorter half life to be taken for an acute exacerbation e.g.ibuprofen, aspirin[4].*

TableE 2. Mean plasma half-lives (SD)* of different NSAIDs.

Short half-life	Half-life (h)	Long half-life	Half-life (h)
Aspirin	0.25 (0.03)	Azapropazone	15 (4)
Diclofenac	1.1 (0.2)	Diflunisal	13 (2)
Etodolac	3.0; 6.5 (0.3)**	Fenbufen	11.0
Fenprofen	2.5 (0.5)	Nabumetone	26 (5)
Flufenamic acid	1.4; 9.0**	Naproxen	14 (2)
Flubiprofen	3.8 (1.2)	Oxaprozin	58 (10)
Ibuprofen	2.1 (0.3)	Phenylbutazone	68 (25)
Indomethacin	4.6 (0.7)	Piroxicam	57 (22)
Ketoprofen	1.8 (0.4)	Salicylate	2-15***
Pirprofen	3.8; 6.8**	Sulindac (sulfide)	14 (8)
Tiaprofenic acid	3.0 (0.2)	Tenoxicam	60 (11)
Tolmetin	1.0 (0.3); 5.8 (1.5)**		

* SD, standard deviation.
** Elimination occurs in two phases (indicated by semicolon), of which the first is generally the most important.
*** Elimination of this drug is dose-dependent.
Reproduced from: Brooks PM. Clinical management of rheumatoid arthritis. Lancet, 1993;341:286-290.

Patients differ in their response to different NSAIDs

Sometimes a patient receiving one NSAID and not feeling any better with it starts improving when another NSAID is added to the regimen. In such situations the physician may erroneous conclude that the combination therapy has worked. The fact is that large variations are possible in the response of individuals to different aspirin-like drugs, even when they are closely allied members of the same group[16]. And in this instance, the patient might simply have responded to the added drug.

Selecting an NSAID for an individual patient, therefore, remains more of an art than a science. Whenever prescribing an NSAID the previous experiences of the patient with

these drugs should always be taken into account and treatment should be started with a low dose of a single drug. The dose can be increased to the recommended maximum over a period of one to two weeks, if needed. If results are disappointing, an alternative NSAID can be tried (while discontinuing the first). One should not keep on changing the NSAID simply because too many of them are available in the market and also discourage the patient from doing so.

Table 3. Antiinflammatory effect of different NSAIDs*.

WEEK ANTIINFLAMMATORY EFFECT
- Paracetamol

MILD TO MODERATE ANTIINFLAMMATORY EFFECT
- **Propionic acid derivatives:** Fenbufen, fenoprofen, flurbiprofen, ibuprofen, indoprofen, ketoprofen, naproxen.
- **Fenamic acid derivatives:** Mefenamic acid.
- **Non-acid drug:** Nabumetone (but its major active metabolite is an acid and a potent inhibitor of prostaglandins).

STRONG ANTIINFLAMMATORY EFFECT
- **Salicylic acid derivatives:** Aspirin, benorylate, diflunisal, salsalate.
- **Pyrazolone derivatives:** Azapropazone, oxyphenbutazone, phenylbutazone.
- **Acetic acid derivatives:** Diclofenac, etodolac, indomethacin, sulindac, tiaprofenic acid, tolmetin.
- **Oxicam derivatives:** Piroxicam, tenoxicam.

*There is some overlap of the groups since effect also depends on dose but the classification broadly holds true.

Reproduced from Laurence DR, Bennett PN. Clinical pharmacology. Edinburgh: Churchill Livingstone. (7th ed.) 1992. p215.

Adjuvant drugs for pain control

Adjuvant drugs are not themselves analgesics but are used alongside analgesics in the management of pain. Examples include: corticosteroids, to relieve inflammation; smooth and skeletal muscle spasmolytics, to relieve the spasm; and psychotropics (anxiolytics and antidepressants) to modify the perception or concomitants of pain like anxiety, fear, depression.

Use of adjuvant for control of pain requires a clear understanding of the cause of pain and clinical experience with these drugs. Indiscriminate use of these drugs with a hope that they will relieve any pain will usually prove ineffective and result in numerous serious side effects these drugs can potentially cause.

Combination products of analgesics

Analgesics are also available as combination products that either contain a mixture of analgesics or combine an analgesic with some other drug. Use of such combination products is not recommended. According to the American Medical Association, although mixtures of analgesics or of analgesics with other classes of drugs are among the most widely used pharmaceutical products relatively few well controlled studies have been performed to determine their comparative effectiveness[17].

Compound analgesic preparations containing paracetamol or aspirin with a low dose of an opioid analgesic are commonly used but the advantages have not been substantiated. The low dose of the opioid may be enough to cause opioid side-effects (in particular, constipation) and can complicate the treatment of overdosage yet may not provide significant additional relief of pain[18].

Compound analgesic preparations containing a full dose of opioid component are effective but carry the full range of opioid side-effects (including nausea, vomiting, severe constipation, drowsiness, respiratory depression, and the risk of dependence on long term administration). When a patient requires both the analgesics simultaneously, instead of giving such a compound preparation, it is more appropriate to give single ingredient products so that both the drugs can be handled independently.

The combination of paracetamol with pentazocine is irrational. When given orally, pentazocine has relatively weak and unpredictable analgesic activity. In both acute and chronic pain, other analgesics have been found to be equally or more effective and with fewer adverse effects than pentazocine[19].

Caffeine, a weak stimulant is also included in small doses in some compound analgesic preparations. It does not contribute to the analgesic or antiinflammatory effect of the preparation and may possibly aggravate the gastric irritation caused by aspirin[18].

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Chapter 13

Antiepileptics - Combination Therapy Is Not More Effective

Seizures are paroxysmal spells of transitory alterations in consciousness or in other cerebral cortical functions. They may result from episodic neurological, psychiatric, or cardiovascular dysfunction. The term epilepsy refers to those seizures that result from paroxysmal and abnormally synchronous discharges of cerebral cortical neurons that are induced by systemic or neurologic disturbances.

Many types of seizures have been identified which are classified according to a scheme developed by International League against Epilepsy (ILAE). The ILAE classification recognizes two broad categories of seizures[1,2] (Table 1):

1. Those that arise in part of one cerebral hemisphere and are accompanied by focal electroencephalographic abnormalities are called focal or partial seizures. Partial seizures produce symptoms that are referable to the region of cerebral cortex primarily involved. In simple partial seizures consciousness remains intact while in complex partial seizures focal events are accompanied by impaired consciousness

2. Those with clinical and electroencephalographic manifestations that indicate essentially simultaneous involvement of all or large parts of both cerebral hemispheres from the beginning are called generalized onset seizures. Generalized seizures consistently cause altered consciousness and may be convulsive (tonic, clonic, tonic-clonic seizures) or nonconvulsive (absences, myoclonic seizures, and drop attacks).

The localized seizure activity in the cerebral cortex often spreads; simple partial seizures may thus evolve into complex partial seizures, and both may evolve into secondarily generalized seizures.

Epileptic seizures are also divided into primary and secondary types. Primary (idiopathic) epileptic seizures are usually inherited, often age related, commonly benign, and not associated with identified structural lesions. Secondary (symptomatic) epileptic seizures result from an identifiable underlying disease or lesion of the brain.

Table. 1: International classification of epileptic seizures.

I. Partial (focal, local) seizures.
- A. Simple partial seizures.
- B. Complex partial seizures.
  1. With impairment of consciousness at onset.
  2. Simple partial onset followed by impairment of consciousness.
- C. Partial seizures evolving to generalized tonic-clonic convulsions (GTC).
  1. Simple evolving to GTC.
  2. Complex evolving to GTC (including those with simple partial onset).

II. Generalized seizures (convulsive or nonconvulsive).
- A. 1. Absence.
  2. Atypical absence.
- B. Myoclonic.
- C. Clonic.
- D. Tonic.
- E. Tonic-clonic.
- F. Atonic.

III. Unclassified epileptic seizures (including some neonatal seizures).

Reproduced from Mattson RH. General principles: selection of antiepileptic drug therapy. In: Levy RH, Dreifuss FE, et al (ed.). Antiepileptic drugs. New York: Raven Press Ltd. 3rd ed. 1989. p104.

Management Of Epilepsy

Epilepsy, in one form or another, affects 4-10/1000 of general populations[3]. It afflicts more than 50 million people worldwide, 5 million of whom have seizures more than once per month[4] It is one of the crippling and incapacitating diseases but if treated properly can be controlled effectively in most instances. Whereas most of the secondary epilepsies (epileptic fits occurring due to some underlying cause e.g, febrile fits, intracranial space occupying lesions etc) can be remedied by treating the underlying cause and rarely need antiepileptics on long term basis, the more common idiopathic fits require long term antiepileptic therapy.

Foremost in managing epilepsy is to reach the diagnosis with a reasonable certainty; misdiagnosis is an important reason of treatment failure. This requires a sound knowledge and clinical understanding of various types of seizures (both epileptic and nonepileptic). The distinction between an epileptic disorder and other systemic conditions (e.g.,hypoglycemia or cardiac arrhythmia), neurological disorders (e,g.,transient ischemic attack or migraine event) or some psychiatric conditions can be difficult, particular when nonepileptic paroxysms occur along with epileptic seizures.

A clear history obtained from the patient and those who may have observed the patient's paroxysmal event provides the best guide to the nature of an episode. Elelectroencephalography (EEG) is the most helpful laboratory test in the diagnosis of epileptic seizures. Nevertheless, an abnormal EEG is not adequate for the diagnosis of epilepsy, and a normal EEG does not rule out the diagnosis[2]. In case of doubt it is prudent to admit the patient (or refer him to such a facility) so that he can be observed, evaluated, and investigated.

Selection of an appropriate antiepileptic drug

Many drugs are available to treat epilepsy and are referred to as antiepileptic drugs. The common ones are listed in Table 2 along with their usual adult dose, therapeutic range of plasma concentration, and important side effects.

Table 2: Antiepileptic drugs.

Drug	Adult dose (mg/24 Hrs)	Plasma therapeutic range (umol/l)	(ug/ml)	Side effects
Carbamazepine	800-1600	34-51	8-12	Drowsiness, blurred vision, diplopia, dysequilibrium, leukopenia, hepatic failure.
Phenytoin	300-400	40-80	10-20	Ataxia, dysarthria, gingival hypertrophy, hirsutism, acneiform eruption, hepatic failure, osteomalacia.
Phenobarbitol	90-180	65-150	15-35	Sedation, depression, loss of concentration, mental dulling, hyperactivity.
Primidone	750-1250	23-55	5-12	Sedation, dizziness, nausea, ataxia, depression.
Valproate	1000-3000	350-830	50-120	Gastrointestinal upset, weight gain, hair loss, tremor, thrombocytopenia, liver failure, pancreatitis.
Ethosuximide	750-1500	280-719	40-100	Gastrointestinal upset, mood changes, lethargy, hiccups, headache.

Adapted from Scheuer ML, Pedley TA. The evaluation and treatment of seizures. In: Desforges JF (ed.). Current concepts N Engl J Med. 1990;323:1468-1473.

The various antiepileptic drugs differ in their relative efficacy for different types of epileptic seizures. Simply prescribing one of these at random may not give the desired therapeutic results. To prescribe anti pileptics effectively and rationally, therefore, one should know the relative efficacy of different antiepileptics for different types of seizures (Table 3).

Table: 3. Drugs used in treating different types of seizures.

Type of seizure	Drugs
Simple and complex partial	Carbamazepine, phenytoin, primidone, phenobarbitpol.
Secondarily generalized	Carbamazepine, phenytoin, primidone, phenobarbitol, valproate(?)
Primary generalized seizures	
Tonic-clonic	Valproate, carbamazepine, phenytoin,
Absence	Ethosuximide, valproate.
Myoclonic	Valproate, clonazepam.
Atonic	Valproate, clonazepam, ethosuximide.

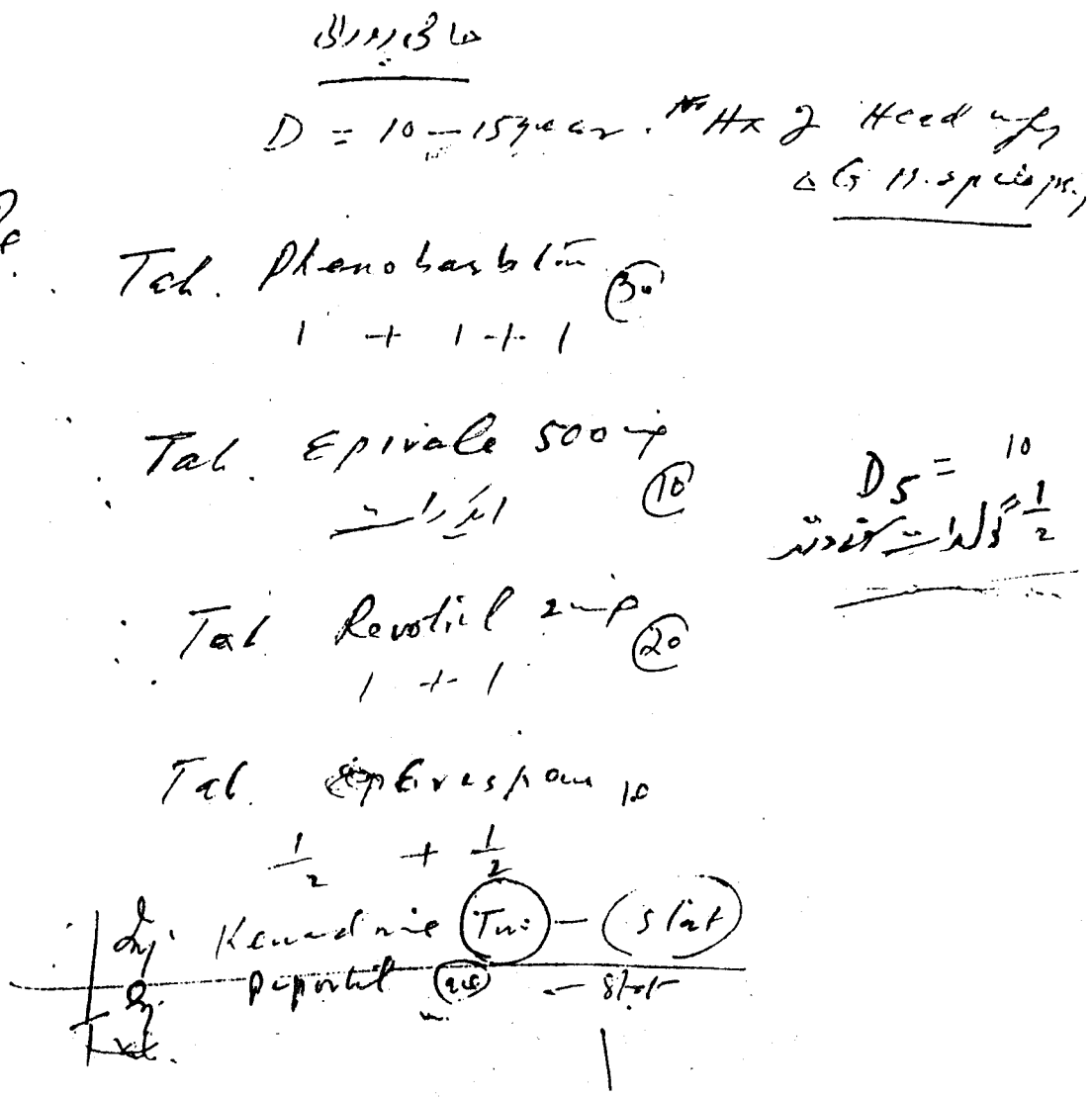
Reproduced from Scheuer ML, Pedley TA. The evaluation and treatment of seizures. In: Desforges JF (ed.). Current concepts. N Engl J Med. 1990; 323:1468-1473.

Carbamazepine, phenytoin, and phenobarbitone are equally effective for partial and secondarily generalized epilepsies. Despite their equal antiepileptic potency, however these drugs differ substantially in their side effects, and it is this factor, together with their pharmacokinetic properties and cost that determines the choice of drug for an individual patient. Thus, phenytoin, that because of its relatively long half-life can be taken once or twice a day, may be preferable to some patients to carbamazepine which needs to be administered more often. Concern about phenytoin's occasional undesired cosmetic effects makes carbamazepine the drug of choice for other patients. Phenobarbitone, because of the high incidence of sedation and cognitive side effects at therapeutic doses is best avoided as an initial therapy.

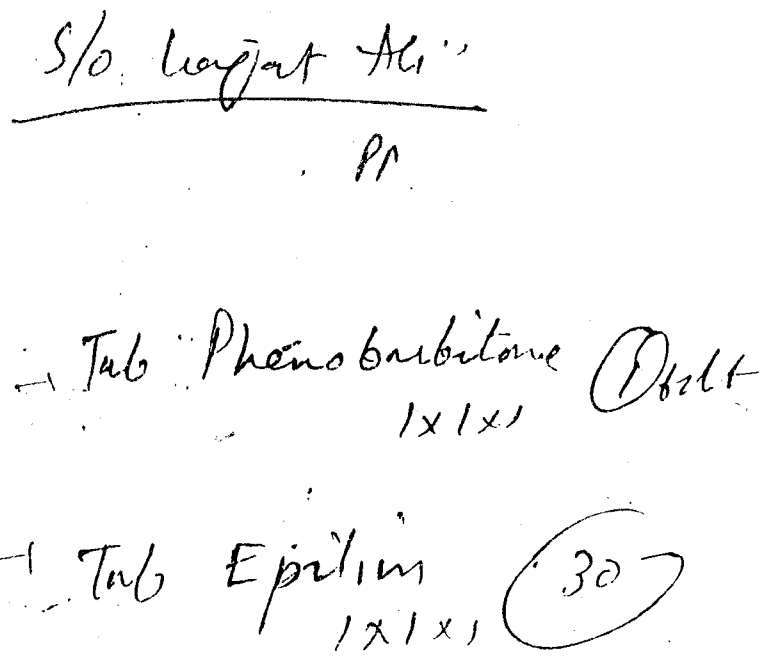
As a group, generalized-onset seizures respond best to valproate. Phenytoin and carbamazepine are also effective against generalized tonic-clonic seizures, but response is less reliable than with valproate[1] Benzodiazepines, specially clonazepam, may be useful in treating myoclonic seizures. Clobazam, another benzodiazipine, has been found to help control intractable epilepsy when it is given in combination with other antiepileptics[5] Ethosuximide is as effective as valproate for absence seizures and has fewer side effects. It is therefore the drug of choice when absence seizures are the only type present.

Is combination therapy with antiepileptics more effective

Early diagnosis and treatment with a single appropriate agent is now the preferred method of treatment for epilepsy and offers the best prospect of achieving prolonged seizure free periods with the lowest risk of toxicity[4,6]. Majority of seizures can and should be controlled with a single drug[7]; beginning therapy with multiple drugs is irrational (Prescription 1 & 2). It may expose the patient to increased risk of drug toxicity without any added therapeutic advantage[8]. In a nation-wide study in Great Britain, monotherapy resulted in satisfactory control of seizures in about 60 percent of patients. Of those in whom the first drug was ineffective, 55 percent responded to



PRESCRIPTION 1. Three antiepileptics (phenobarbitone, valproic acid, and clonazepam) have been prescribed concomitantly. Erispan, being a benzidaizepine, may also have some antiepileptic effect but not in the dose in which it has been prescribed; perhaps it has been prescribed as an anxiolytic. Such a combination therapy is usually not more effective than monotherapy and effort should be made to control the fits with a single appropriate antiepileptic by gradually increasing its dose to the upper recommended level.



PRESCRIPTION 2. The prescription contains a combination of two antiepileptics (phenobarbitone and sodium valproate). Though age of the patient is not written on the prescription, it appears that the treatment has been suggested to a child (because instead of patient's name, his father's is written on the prescription). Provided the patient is a child, the dosage of both the antiepileptics are optimal. However, if a patient's fits are not getting controlled with the full doses of a single antiepileptic, it should be substituted with another; two antiepileptics should be used simultaneously only when a patient has not responded to full doses of different antiepileptics of choice when given alone.

an alternative drug when used alone. Of the remaining patients only half had better control of seizures with two drugs[1]. Another large study showed that addition of a second anti-epileptic drug achieved total seizure control in only 11% of patients, whereas toxicity developed in 90% of patients[4].

As discussed above, each type of fit has a first line of therapy to which it is more likely to respond. The preferred therapy for recurrent epileptic seizures is the administration of a single anti-epileptic drug that is most appropriate for the type of the seizure. The drug should be used in sufficient doses to control the seizures as fully as possible. If side effects become intolerable before the seizures are adequately controlled, the drug should be replaced by another medication, also used alone, until single drug therapy clearly fails. Treatment with more than one drug is usually less effective, because drug interactions impair effectiveness and side effects accumulate[2].

Only when monotherapy with all appropriate drugs have failed to control seizures should combination treatment be tried[1,4]. When a single drug fails to provide adequate control of seizures its dose has to be increased to the maximum recommended or tolerated level. Adding another antiepileptic without increasing the dose of first to a maximal level is not advisable and is irrational. Even when a single drug fails to provide control of seizures in maximal tolerated dosage, and if compliance has been confirmed, another drug should be substituted[9]. During the process of substitution a second antiepileptic is added to the first temporarily. While the dose of the second antiepileptic has been increased to a maximum the first is then gradually tapered off. If the first drug has produced partial control of the seizure disorder, however, it is often continued with the second drug[8].

Generally it is recommended to treat seizures with one or a maximum of two anticonvulsants, if monotherapy with first line anticonvulsant is ineffective. There is no place for therapy with more than two drugs[10]. Indiscriminate combination of antiepileptics is a naive and irrational approach to control seizures (Prescription 1). Polytherapy increases the risk for drug interactions, teratogenecity, and adverse effects; makes monitoring more difficult; and results in decreased patient compliance. It also results in aggravation of seizures in some patients. Conversion of polytherapy to monotherapy may improve seizure control and mental performance[11]. One study showed that converting the therapeutic regimen from combined therapy to monotherapy produced no increase in seizures in 83% of patients and produced a decreased frequency of seizures in 36%. In another study, patients who were converted to monotherapy showed a 55% improvement in cognitive function, particularly alertness, drive, mood, concentration, and sociability[4]. Even if polytherapy has given good seizure control, it is not justifiable unless a proper trial of monotherapy has proved unsuccessful.

Noncompliance - an important reason for therapeutic failure

One of the major causes of uncontrolled seizures is the failure of the patient to follow the prescribed regimen[12]. It has been estimated that one third to one half of patients

with epilepsy do not comply with their treatment regimens[2]. No association exists between noncompliance and factors such as age, sex, level of education, and duration of disease. However an association has been established between noncompliance and the number of concurrent medicines prescribed (see chapter 6 for details). Noncompliance is clearly higher in patients requiring combined antiepileptic drug medication than in patients receiving monotherapy. Noncompliance also increases when patients misunderstand instructions for using prescribed medicine.

Box 1: Improving compliance with antiepileptic drugs.

There are several ways to improve compliance. Even with complicated regimens, compliance is possible if the patient is capable of learning.

1. For patients who seem apathetic about their problems, emphasize the importance of taking prescribed doses so that the physician can interpret the results of therapy.
2. Be understanding and forgiving but firm with patients who are capable of good compliance. At the first visit, it may be useful to reach an understanding of the importance of regular drug intake. Compliance is a reasonable price to pay for improved seizure control, and the physician should expect it.
3. Ask frequently about drug compliance. Have the patient (or guardian who manages the pills) recite, at each visit, the number of each tablet taken and when each is taken during the day. The patient will come to expect the question and will therefore learn the daily regimen. Since alternate day regimens (e.g., 300 and 400 mg of phenytoin on alternate days) are unnecessary and a good excuse for getting confused, they should not be used (instead e.g., give 350 mg/day of phenytoin).
4. An effective technique for improving compliance, and one that the physician should insist on in difficult cases, is the "morning set-up plan. Insist that the patient (or the guardian) count out the entire day's dose of medications on awakening in the morning; place the tablets in the designated place such as a cup or a separate pillbox. Draw from this receptacle as needed for the day's dose and inspect it at bed time to be sure the day's dose is entirely consumed. Repeat the procedure each day. Well-educated patients will resist such an elementary procedure; ignore these complaints and insist that it be followed.

"Reproduced from: Porter RJ. General principles: how to use antiepileptic drugs. In: Levy RH, Dreifuss FE. Antiepileptic drugs. New York: Raven Pres Ltd. 3rd ed. 1989. p125-126."

Therefore, it is essential to thoroughly evaluate for drug compliance whenever epilepsy is not getting controlled. To increase the dose or change the medicine without confirming compliance to treatment is not beneficial and can be considered as a careless therapeutic approach. Whereas, in most cases compliance to treatment can be assessed by a calm and detailed inquiry, in case of doubt serial blood levels can be used to assess it. Whether assessing compliance or obtaining levels for other reasons, levels should always be drawn at the same time of the day and preferably at trough, that is, just before the dose. This is particularly true for drugs with short half lives. Table 3 gives the half lives and the therapeutic range for various antiepileptics.

It should be remembered that the therapeutic range is the range within which most patients have a therapeutic effect without having symptoms of toxicity. These ranges are only the most basic guideline. Patients may become seizure-free at so called sub-therapeutic levels or may have toxic reactions at levels within the therapeutic range; this is particularly true for patients on polytherapy[4]. Whenever it is found that poor compliance is the reason for poor seizure control attempt should be made to improve it (Box.1).

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Chapter 14

VITAMINS - OFFER NOTHING TO HEALTHY PEOPLE

Vitamins are organic compounds that are needed in small amounts to promote one or more specific biochemical reactions in the body. They act as catalysts and coenzymes to complete an enzyme system and do not provide calories to the body. Because they cannot be synthesized in the body, either at all or in amounts sufficient to meet the body requirements, they have to be essentially supplied in diet.

So far thirteen compounds have been identified as vitamins for the humans[1,2]: vitamins A, D, E and K are fat soluble; vitamins C (ascorbic acid), B_1 (thiamine), B_2 (riboflavin), B_3 (niacin), B_5 (pantothenic acid), B_6 (pyridoxine), B_{12} (cobalamin), biotin (vitamin H) and folic acid are water soluble.

Vitamin claims have been made for carnitine (as vitamin B_7), bioflavonoid agents (as vitamin P), choline, lecithin, para-amino-benzoic acid, and inositol. These substances, however, do not fulfil the criteria of a vitamin. They are usually abundant in the diet, can be synthesized in the body, and have not been proved to be essential in human nutrition because deficiency symptoms have never been reported[2].

Some vitamins can be synthesized in the body but the quantities are not sufficient to meet the body requirements. Some of vitamin D required can be formed by the action of sunlight on the compound, 7-dehydrocholestrol, which is present in skin. Some of the niacin required can be formed from the amino acid, tryptophan, and some of vitamin A require can be formed from the beta-carotene present in some vegetables. Intestinal bacteria make most of the vitamin K and some of the biotin and pantothenic acid required.

Vitamins are absorbed and distributed to tissues where they are used. Excess of water soluble vitamins are excreted in urine, except for vitamin C, limited amount of which are stored in leucocytes and platelets. Excess of vitamin A and D are deposited mainly in liver and vitamin E in adipose tissue.

Who need vitamin supplements

Vitamin supplements are needed only by persons who have deficiency of vitamin/s or are vulnerable to develop such a deficiency. Healthy people do not require or benefit from such supplements (see below).

The role of vitamins in regulating body processes and in maintaining health are well known. Symptoms and signs of their deficiencies have been documented and well described. The use of vitamins is advisable in circumstances where such deficiencies exist or are likely to occur. Such vitamin/s deficiency states may arise from inadequate intake , malabsorption, increased tissue needs, or inborn errors of metabolism (3).

Inadequate intake

Dietary deficiency whether due to poverty, erroneous dietary beliefs, food faddism, or anorexia can lead to deficiency of vitamins and other nutrients. While correction of the deficiency state may need therapeutic administration of vitamins and minerals, it is more appropriate to encourage the patient to take a balanced diet instead of vitamin/mineral preparations as a long term intervention.

Dietary deficiency and malnutrition as a consequence of poverty is a common problem of many developing countries. But it needs to be realised that malnutrition is not treatable at all by drugs - it is treated with food. The growing dependence on vitamin and mineral tonics can have a damaging impact on the nutrition of the poor. This is the case when they spend money on tonics instead of food. It can even present problems when they do not have to buy them[4]. The poor is likely to consider the prescribed vitamins a substitute of and buy them at the expense of foods like milk, fruits, and meat. It is more rational to give dietary guidance to such a patient according to his resources (Table 1).

When nutritional deficiency is a result of erroneous dietary beliefs or food faddism a rational approach is to improve the dietary habits through education. Prescribing such patients vitamin and mineral tonics prophylactically will add to their erroneous beliefs - vitamins are a substitute for food they do not take.

For anorexic, malnourished patients therapeutic significance of vitamins cannot be denied but by prescribing vitamins the job is not complete. Effort should be made to find out the cause of anorexia and treat it (it is not a good practice to improve appetite by giving appetite-stimulants;see chapter 15 for details).

Intestinal malabsorption states

Therapeutic administration of vitamins may be needed in malabsorption disorders; examples include: hepatobiliary and pancreatic diseases, prolonged diarrhoeal illness, hyperthyroidism, pernicious anaemia, and intestinal bypass operations. Moreover, since a substantial proportion of vitamin K and biotin is synthesized by the bacteria of the gastrointestinal tract, treatment with the antimicrobial agents that alter the intestinal bacterial flora inevitably leads to decreased availability of these vitamins.

Increased body requirements

Increased tissue requirements for vitamins may cause a nutritional deficiency to develop despite the ingestion of a diet that had previously been adequate. Examples include hyperthyroidism, conditions accompanied by fever or tissue wasting, pregnancy and lactation. In such instances vitamin/mineral supplements may be needed to correct the deficiency.

Table 1: Dietary sources of vitamins.

Vitamin	Dietary source
Vitamin A	Liver, cream, butter, and egg yolk. Yellow and green vegetables and fruits are good dietary sources of the carotenes, which serve as precursors of vitamin A
Vitamin D	Fatty fish, eggs, liver, and butter (milk, unless fortified, is not a good source of the vitamin)
Vitamin E	Vegetable oils are rich sources. Liver, eggs, and green leafy vegetables contain moderate amounts
Vitamin K	Cabbage, cauliflower, spinach, egg yolk, and liver. (Large amounts of the vitamin are synthesized by the intestinal bacteria)
Thiamine (B_1)	Grains and legumes are the richest source; outer layers of seeds are particularly rich in the vitamin
Riboflavin (B_2)	Milk, eggs, liver, and green leafy vegetables are good source of the vitamin
Niacin (B_3)	Found in unrefined grains and cereal, milk, and lean meats, specially liver (limited quantities can also be obtained from the metabolism of tryptophan)
Pantothenic acid (B_5)	Vitamin is widely distributed; eggs, liver, and yeast are the richest sources
Pyridoxine (B_6)	Good sources are wheat, corn, egg yolk, liver, and meat
Cobalamin (B_{12})	Present in appreciable amounts in liver, whole milk, eggs, chicken; not present in vegetables
Biotin	Present in almost all foods, particularly liver, egg yolk, and milk
Folic acid	Found in green leafy vegetables, whole grain cereals, and liver
Ascorbic acid (C)	Citrus fruit, potatoes (particularly in their skin), tomatoes, and green vegetables are good source

Is it rational to prescribe vitamins to healthy people?

Healthy persons eating a healthy (adequate and balanced) diet do not need vitamin supplements[5] and do not benefit from them[6]. The American Institute of Nutrition and Society for Clinical Nutrition recommends[1]:

"Healthy children and adults should obtain adequate nutrient intakes from dietary sources. Meeting nutrient needs by choosing a variety of foods in moderation, rather than by supplementation, reduces the potential risk for both nutrient deficiencies and nutrient excesses. Individual recommendations regarding supplements and diets should come from physicians and registered dietitians."

And according to the British Medical Association[1]:

"Vitamin supplements should not be used (or advised) as a general tonic to improve well-being - they do not do so - nor should they be used as a substitute for a balanced diet."

In spite of these scientific recommendations vitamins are extensively prescribed to and used by healthy persons. This is partially due to the ready availability of these substances, their advertisement by a growing number of vitamin enthusiasts whose motivation is primarily profit-oriented, the lack of information on the distinction between sufficient and excessive vitamin use, and the failure of the scientific community to communicate effectively with the public[2].

The pharmaceutical industry bas been promoting the sale of their vitamin preparations claiming them to be effective and beneficial for a wide variety of day to day symptoms like tiredness and fatigue, lethargy, poor appetite, loss of energy, and poor concentration and to promote growth and intelligence of children, and to cure infertility. These claims are not supported by scientific evidence[7] but they have adversely influenced the concepts of the prescribers and beliefs of the consumers. As a leading book on pharmacology comments, "the indiscriminate use of vitamins is widely advocated by pharmaceutical companies and practised by the gullible[8]."

An important reason for taking vitamin supplements is the erroneous belief that such preparations provide extra energy and make one 'feel better[3]. Easy and widespread availability of these compounds has further led to there inappropriate and unnecessary use. According to Laurence's Clinical Pharmacology, "it has often been suggested, but never proved that subclinical vitamin deficiencies are a cause of much chronic ill-health and liability to ill health. This idea has led to enormous consumption of vitamin preparations, which, for most consumers, probably have no more than a placebo value. Fortunately most of the vitamins are comparatively non-toxic, but prolonged administration of vitamins A and D can have serious ill effects[9]".

Mega-doses of vitamins - are they of any benefit?

Large (mega) doses of vitamins are claimed to be of therapeutic and prophylactic value for a wide variety of conditions such as common cold, premenstrual tension, central and peripheral nervous system disorders, bone and joint diseases, mental and behavioral disorders, and cardiovascular disorders. These claims are not supported

Table 2: Scientifically unsubstantiated claims made for mega doses of vitamins and the likely adverse effects of over-dose*.

Vitamin	Claims made for mega-doses	Adverse/toxic effects
Vitamin A	Mega-doses of beta-carotene and vitamin A are protective against lung cancer.	Anorexia, dryness and scaliness of skin. Loss of calcium from long bones concomitant hypercalcemia, raised serum alkaline phosphatase, and increased intracranial pressure mimicking the symptoms of brain tumor. Enlarged liver and increased ESR. Teratogenicity.
Vitamin D	Higher doses (5-10 times the 1980 RDA) will help build stronger bones.	Nausea, headache, loss of appetite, weakness and fatigue. Damage resulting from calcium deposits in kidney and other soft tissue. Interference with absorption of vitamin K. Hypercalcemia in breast-fed infants.
Vitamin E	Mega-doses increase sexual potency and cure infertility. Prevent mental retardation, heart disease. and prolong life.	Can interfere with vitamin K metabolism and result in haemorrhage. Some reports have implicated large doses of vitamin E as a cause of thrombophlebitis. Decreases rate of wound healing in animals and causes gastrointestinal distress and creatinurea in humans.
Vitamin K	No such claim made yet.	Vitamin K has been overlooked by vitamin enthusiasts; a few reports are available on the adverse effects of the natural vitamin.
Vitamin B complex	Claims have been made for the use of mega-doses of thiamine and niacin to improve central nervous system disorders, to prevent age associated deterioration and to cure mental illness. Vitamin B_6 mega-doses, claimed to improve premenstrual edema, behavioral disorders andneurological dysfunction.	These mega-doses have resulted in liver damage, exacerbation of peptic ulcers and in the case of niacin, a histamine flush. Have actually caused severe nervous system dysfunction and liver damage.
Vitamin C	Mega-doses have been claimed to prevent common cold, promote wound healing, reduce the intensity and severity of heart disease, and has a possible role in cancer prevention and cure.	May cause diarrhoea and formation of oxalate stones in kidney and bladder. Can interfere with absorption and metabolism of vitamin B_{12}, which cannot be remedied by vitamin B_{12} supplements. When given to pregnant women may predispose the new born to scurvy.

Adapted from; Henry J. The British Medical Association guide to medicines & drugs. London: Dorling Kindersley Limited, (2nd ed.), 1991. p145. And Alfin-Slater RB. Vitamin use and abuse in elderly persons. In: Morley JE, moderator. Nutrition in the elderly. Ann Intern Med. 1988;109:890-904.

by scientific evidence; in fact mega-doses of some of the vitamins may lead to adverse and toxic side effects[2,10,11] (Table 2). Therefore, prescribing vitamins to prevent or speed up recovery from these conditions is not rational.

Do vitamins improve intelligence of children?

Another claim regarding vitamin and mineral supplements is that when they are given to children their intelligence and reasoning abilities improve. Children with clinical deficiency states will definitely benefit from supplements in this regard. Nevertheless, it seems improbable that any marginal nutrient deficiency will effect the metabolic functions of the brain because vitamins and minerals are transported from the blood to the brain by specific active mechanisms and homeostasis of micronutrients occur in the central nervous system[11]

First study that supported the claim was reported in the UK in 1988[13], however, the study was found to have many weaknesses[14,15,16,17,18,19] and two attempts to confirm the results failed[12,20]. Since then numerous studies have been conducted in this regard but "the case for vitamin and mineral supplementation as a method of increasing child's IQ remains unproven[21]".

Few comments on available vitamin preparations

Vitamins (and minerals) are either used for therapeutic purposes in specific deficiency states or prophylactically as supplements. Vitamin preparations intended for therapeutic use should preferably contain a vitamin or vitamins from specific groups in amounts higher than those recommended as a daily allowance. Those intended for use as supplements should contain individual ingredients in amounts sufficient to meet recommended daily allowance (RDA). In addition, inclusion of agents that have no proved value (e.g. choline, methionine, lecithin, bioflavonoids, inositol, biotin, pantothenic acid) in these preparations is unwarranted[22,23].

Numerous vitamin preparations are available throughout the world. Many of these preparations do not qualify to be used for therapeutic or prophylactic purposes; they contain non-essential ingredients, the formulation is irrational and/or dose is excessive (Table 3). Therefore, for rational prescribing of vitamin/mineral preparations, simply being familiar with the proprietary names of the products is not enough; it is essential know the details of the ingredients of the formulation as well.

To conclude

1. Only thirteen compounds have been established as vitamins (vitamins A, D, E, K, C, B_1, B_2, B_3, B_6, B_{12}, pantothenic acid, biotin, and folic acid. Other compounds promoted by the pharmaceutical industry are not vitamins and their deficiency state has not been recognized in humans.

Table 3. Vitamins on sale in selected markets

Description	Pakistan		Middle East		Africa		Caribbean	
	No.	%	No.	%	No.	%	No.	%
Total no. of vitamins	263		195		94		84	
Indications								
For therapeutic use	94	35.7	111	56.9	60	63.8	58	69.1
Prophylaxis/supplement	172	65.4	85	43.6	33	35.1	23	27.4
Unproven indications	109	41.4	140	71.8	67	71.3	62	73.8
Formulation								
Non-essential ingredients	96	36.5	99	50.8	41	43.6	34	40.5
Irrational formulation	122	46.4	125	64.1	55	58.5	54	64.3
Excessive dosage	120	45.6	95	48.7	39	41.5	32	38.1
Not recommended	204	77.6	175	89.7	84	89.4	70	83.3
Total vitamins all ares 636								
Total not recommended 533 (83.8%)								

Sources: QIMP Pakistan (1990); MIMIS Middle East (1990); MIMS Africa (1991); MIMS Caribbean (1991).

Reproduced from: Chetley A/Health Action International. Problem drugs. Health Action International: the Netherlands, Amsterdam. 1993. p123.

2. Vitamin deficiency may result from inadequate dietary intake, intestinal malabsorption conditions or as a consequence of increased bodily requirements. In these conditions therapeutic use of vitamins may be justified and rational.

3. Even in a vitamin deficiency state, specially when it is a consequence of inadequate dietary intake due to under-nutrition or bad dietary habits, a sincere effort should be made to correct the deficiency by providing dietary guidelines to the person.

4. Vitamin supplements have not been found to be of any benefit for nonspecific symptoms like tiredness, fatigue, lethargy, poor appetite, poor concentration, vague body aches, and decreased libido. Their use to treat such symptoms is not rational.

5. Vitamin supplements offer nothing to healthy people and their use by healthy people, specially those taking an adequate diet, should never be encouraged.

6. Vitamin supplements do not increase the intelligence of children. vitamins, therefore, should never be prescribed for this purpose.

7. Claims have been made that mega-doses of some vitamins are effective in controlling or curing certain illnesses. These claims, however, have generally been not been substantiated by scientific evidence. One should not get carried away by such amazing claims of the manufacturers.

8. Most of the vitamin and mineral combination products available in the market are inappropriate and irrational. Doctors, therefore, should be familiar with the composition of various preparations and prescribe the ones that have a rational formulation and do not contain unessential compounds.

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Chapter 15

Medicines - Not All Are Useful And Effective

During last few decades numerous drugs have been developed and drug manufacturing and marketing has evolved into a huge industry. This flood of new drugs in recent years has provided many dramatic improvements in therapy, but it has also created a number of problems of equal magnitude. Not least of these is "therapeutic jungle", the term used to refer to the combination of confusion over nomenclature and the associated uncertainty of the status of many of these drugs[1].

The pharmaceutical manufacturers, as discussed in chapter 8, are primarily interested in generating profit out of their involvement in business. While they spend millions of dollars in search of new drugs, they have to maintain and preferably improve, the profits to survive and progress. One of the important ways to remain in the competition is to keep on introducing new drugs into the market. In most instances, the new drugs introduced are merely a minor alteration in some existing compounds and do not offer any major advantage over the existing ones and, in fact, some of these may be lesser effective and/or more toxic than the older ones. Being the "new" drugs they are also more expensive. On other instances, drugs are introduced into the market and promoted by the manufacturers with claims that are not supported by any convincing scientific evidence and thus are of doubtful efficacy[2]. Experts describe such drugs in terms like: 'of doubtful efficacy'; 'obsolete'; 'should be avoided' (British National Formulary); 'rarely useful'; 'the risk no way justifies continued use of these drugs'; 'there is no rational for use of these drugs' (American Medical Association Drug Evaluations); 'has been superseded by less toxic compounds'; 'no longer recommended'; 'of no value' (Martindale: The Extra Pharmacopoeia); 'irrational and unsafe therapy'; 'not generally recognized as safe and effective'; 'there is no evidence to support its effectiveness' (US Food And Drug Administration); 'does not seem worth using'; '... has no special virtues and is more expensive'; 'particularly hazardous' (Drug and Therapeutic Bulletin)[3]. As a group all such drugs and preparations can be considered as less acceptable or undesirable that are not essential to maintain the health of humans.

Availability of such useless and undesired drugs is a worldwide problem. As many as 70% of the pharmaceuticals on the world market are considered inessential/or undesirable products that would tend to impair rather than improve health[4]. Over one in five of the 4500 preparations listed in the British National Formulary(1984) were rated less suitable for prescribing. In the USA 8 of the 25 drugs most frequently

prescribed in 1976 were authoritatively considered of questionable value. In the Third World countries, the situation is usually worse. This is partly because doctors there get less reliable information about drugs; and also because government control of medicines tends to be weak[3].

Use of ineffective and less acceptable drugs/preparations leads to treatment failure, exposes the patient to unnecessary side effects and is a waste of their money, and is an avoidable burden on the resources of the country. For rational prescribing, it is essential for the physician to be able to recognize the less acceptable drugs/preparations available on the market and refrain from prescribing them (Box 1).

Box 1: Criteria to distinguish between more or less acceptable drugs.

There is general agreement about the main criteria used to distinguish between more or less acceptable products. Independent experts tend to criticize drugs when:

- drug treatment is unnecessary, undesired or misconceived.
- alternative treatments are likely to be more effective or safer,
- medicines contain ingredients of little or no proven value,
- the product is poorly formulated - e.g., an inappropriate combination of ingredients,
- there is strong evidence of inappropriate use,
- the product offers relatively poor therapeutic value for money.

Reproduced from: Medawar C/Social Audit. Drugs and world health. International Organization of Consumers' Union. Holland: Gravisie, Bodegraven, 1984. p4.

Numerous preparations available in the market meet the criteria of less acceptable drugs; to discuss them individually is not the scope of this book. However, some groups of "less acceptable drugs" in common use are discussed in the proceeding three sections of this chapter.

Brain Tonics - A Fiction Portrayed As A Fact

"Brain tonics" is the term introduced by the pharmaceutical industry for drugs that are being promoted by them, and thus being prescribed by doctors, to improve cerebral functioning. These are claimed to improve cerebral circulation or metabolism and consequently its functioning. They are also called cerebral vasodilators or nootropils, and among others include: encephabol, hydergine, sermion, loftyl and sibellium.

Two types of people feature prominently in advertising for these drugs: children who suffer from lack of attention, poor performance at school, and hyperactivity; and the

elderly who suffer from loss of memory,and dementia In both cases the claims for the drugs suggested for treatment stretch medical findings far beyond medical limits[5]. Such claims have also lead to prescription of such drugs for the third age group - the students to improve their concentration, and people in competitive jobs to improve their performance. Some of the manufacturers extend the claims of usefulness of their preparations to conditions like depression, unsociability, loss of self care, asthenia, anorexia, and dizziness (Box 2).

Box 2: A point to ponder

"SIR,- At a recent meeting in Pakistan, I was told that the urban poor, suffering from diseases associated with overcrowding and polluted water, spend much of their small incomes on useless or inappropriate medicines. Not all of these are "quack medicines" provided by native healers. Some of the worst examples of quackery can be found in advertisements by ethical multinational companies, taking advantage of the fact that drugs can be easily bought from pharmacists and that local drug control legislation is weak or ineffective.

For example, many advertisements for benzodiazepines are untempered by western experience. Sandoz assures that "with Restoril (temazepam) patients do not experience drug dependence". Parke Davis states that "Verstan (prazepam) may provide an advantage in certain patients prone by history to drug misuse". Searle announces that "tranxene extends a helping hand to your worried patients", while Roche claims that 'Lexotanil' (bromazepam) "resolves anxiety and relieves the strain on the heart.... Clinical reports [none of which are listed] confirm that very good results are obtained in angina pectoris, cardiac arrhythmias, palpitations and precordial pain mimicking angina pectoris". These are misleading statements. There are also claims for other drugs which are not part of the UK pharmacopoeia. If these claims are correct, then British doctors and their patients are missing out on a therapeutic revolution.

'Loftyl' (buflomedil), according to Abbott Laboratories, "alleviates symptoms of intellectual deterioration, change of personality, and loss of memory". 'Sermion' (nicergoline) "revitalises cerebral circuitry", and is indicated for "intellectual, affective, behavioral and somatic symptoms associated with cerebral decay (including Parkinson's disease and senile and presenile dementia) as well as for memory disorders, reduced concentration, mood depression, unsociability, loss of self-care, asthenia, anorexia and dizziness". This drug is marketed by Farmitalia Carlo Erba, who state that there is only one contraindication - hypersensitivity to nicergoline. I was told that advertisements of these and similar drugs were to be translated into Urdu and aimed at parents who might be anxious about their children performance at school.

Not all the companies behave in this way. I saw several advertisements providing the sort of information that would be required in the UK. The companies concerned included Wyeth, Glaxo, Reckitt and Colman, and Ciba-Geigy.

What can be done? Proposals for a limited WHO list seem doomed to fail in the open market and the bazaar. Drug companies will weep a few crocodile tears and carry on until effective local legislation arrives to control them."

Reproduced from: Birley JLT. Drug advertisements in developing countries. Lancet, January 28,1989. Page 220

These drugs are widely promoted by the manufacturers for senile dementia and peripheral vascular insufficiency but clinical literature overwhelmingly indicates that these drugs are ineffective for these conditions[6]. According to Goodman and Gilman's Pharmacological Basis of Therapeutics, "the utility of vasodilators in reversing or delaying the deleterious effects of acute or chronic cerebrovascular insufficiency is controversial and the case of clinical efficacy is unproven[7]". According to British National Formulary "these drugs are claimed to improve mental function. Some improvement in performance of psychological tests have been reported but the drugs have not been shown clinically to be of benefit in dementia[8].

The status and efficacy of these drugs is not only doubtful in most instances, in fact, some of them have been clearly been found to be useless and even harmful. Medical Lobby for Appropriate Marketing (MaLAM) has regularly challenged pharmaceutical companies to defend the claims made for the various "brain tonics" on the market (Table 1). To date, the industry has been unable to produce much evidence in its defence. Where companies have responded to MaLAM, the quality of the studies they have used to justify their claims has generally been poor[9].

Table 1. Complaints made by MaLAM about promotion of brain tonics (1986-1991)

Company/Brand Name/ Generic Name	Claims/indications
Abbott/Loftyl/ Buflomedi	Improved memory and concentration, improved reasoning ability, better sleep, improved adaptation to environment. (Pakistan, late 1988)
Bayer/Nimotop/ Nimidopine	"FDA approved", changes in brain function.... such as reduced capacity for concentration and memory, depression, fear, lack of initiative, lack of social contact, dizziness. (Panama, Nov. 1991)
Carlo Erba/ Sermion/ Nicergoline	Symptoms of chronic cerebral insufficiency (Indonesia, June 1988); senile and presenile dementia (Philipines, April 1988)
Hoechst/ Trental/ Oxpentifylline	Prevent recurrent ischemic attacks.... imroves cognitive and mental function (Indonesia, 1990)
Janssen/ Sibelium/ Flunarizine	Lack of concentration, confusion, memory disorder, irritability, safe (Hong Kong, Dec. 1986)
Roussel/ Targifor/ Arginine aspartate	Comprehensive treatment for fatigue and stress... for.... the elderly.... increases concentration.... increases intellectual output (uruguay, 1991)
Sandoz/Hydergine/ Codergocrine	Impressive improvement of the symptoms of cerebral insufficiency (Pakistan, 1986); symptoms of mental decline such as confusion, dizziness, memory lapses (Philipines, 1986)

Reproduced from: Chetley A/Health Action International. Problem drugs. Health Action International: the Netherlands, Amsterdam. 1993. p114.

The maximum these "brain tonics" offer is a placebo effect, but even as a placebo they are not only very expensive but are also likely to cause undesired side effects. The World Health Organization does not consider any of these drugs essential for health of the people of any country and therefore none of them is included in its essential drug list.

In spite of these scientific facts these drugs are widely prescribed, and regrettably sometimes in combinations (Prescription 1). It should be realized that by prescribing these drugs, one is merely acting as an agent of pharmaceutical industry, transferring money from patients' pockets into the pharmaceutical industries account. The prescription of these "marvellous brain tonics" should always be avoided.

Appetite Stimulants - No Place In Rational Prescribing

Loss of appetite is not a primary disease

Loss of appetite is not an uncommon symptom reported by the patients but as such it is not an illness; in fact it is a symptom of wide variety of conditions. Common causes of loss of appetite in children include intestinal worm infestation, recurrent or chronic infectious conditions, malnutrition, bad dietary habits, and emotional deprivation. The elderly may loose their appetite due to various endocrinological and psychiatric illnesses, chronic infections, malignant conditions, renal, cardiac, respiratory and hepatic diseases, and in some instances because of the medicines they are taking for some illness. Sometimes, mere absence of physical activity and bad health and dietary habits or old age are the cause of loss appetite.

Treating loss of appetite

Because loss of appetite is secondary to some underlying illness or is a consequence of bad dietary and health habits, in general little or nothing is gained by stimulating appetite by drugs[10]. The rational approach towards its treatment is to intervene in the underlying cause. Loss of appetite that is secondary to acute but rapidly curable conditions like acute infections, worm infestation, transient gastrointestinal upsets, migraine, is generally easy to reestablish if the condition is effectively treated. Anorexia as a consequence of chronic conditions like malignancy, chronic infections, depression and other psychiatric disorders, and cardiovascular, respiratory and metabolic disorders is generally difficult to manage because of the chronic nature of these conditions and the depression, hopelessness, and helplessness that invariably accompanies them. Reassurance and persistent but polite persuasion, along with the provision of a suitable diet that has a range of taste , flavour, and consistency, can help restore the appetite. Furthermore, a popper course of antidepressants can be of benefit if loss of appetite is accompanied by other features of depression.

10/1/94

① Th. Serenace 5mg
1 + 1 + 1

② Th. Kemadrin 5mg
1½ + 1½ + 1½

③ Th. Nootropil 800mg
1 + 1 + 1

④ Sp. Encephabol

⑤ Inj. Bevidox IM

⑥ Sp. Trans-Oxix Fort

⑦ Sp. Increm

CT-Scan

PRESCRIPTION 1. Many physicians view the "Brain Tonics" as they are portrayed by the manufacturers. Some of them are so convinced of their effectiveness that they may prescribe them in combination!

Loss of appetite in otherwise healthy individuals is usually due to bad health and dietary habits; sedentary life style, lack of physical activity, smoking, excessive use of tea and coffee, predominant use of roasted and fatty diet, excessive use of sweets and sweetened drinks, limited use of fruits and dietary fibre, untimely meals, and erroneous dietary beliefs. A thorough evaluation and appropriate education and guidance can help such individuals recover their appetite if they comply with the instructions.

Various medicines may also cause loss of appetite due to different reasons; metronidazole, by giving a bad taste to the mouth; tricyclic antidepressant, most of antipsychotics (appetite may increase by a central effect), and anticholinergic drugs, by decreasing salivation and gut motility; many antibiotics by altering bowl functioning; analgesics, by giving a heart burn; and almost all the drugs by causing nausea. Therefore it is essential to inquire about the drugs the patient is taking. Simply discontinuing a medicine or modifying the time and pattern of its/their intake may result in improvement of appetite of such patients.

Why use of appetite stimulants is irrational?

In spite of the fact that loss of appetite is secondary event that can best be treated by treating or intervening in the underlying illness or reason, compounds claimed and promoted as appetite stimulants are available in the market (of developing countries) and are being used both through prescriptions and by over the counter purchase. Two such compounds that are available in our country and many other countries of the developing world are: Cyproheptadine (Periactin, Tres-orix Forte) and Pizotifen (Mosegor). Both these compounds are primarily indicated for certain other conditions (see below), to stimulate appetite is one of their transient side effect, and their promotion as an appetite stimulant is not permitted in developed countries where medicines are monitored and regulated more strictly and efficiently. But in the developing countries, the manufacturers of these drugs, unchecked by the regulatory agencies, have so heavily, efficiently and convincingly promoted them as appetite stimulants that it has become the primary indication for prescribing these compounds. Even lay-people now well recognise them as appetite stimulants and many doctors seem to be unaware of their primary and scientifically approved indications!.

Cyproheptadine

Cyproheptadine is an H_1-antagonist with some serotonin blocking activity. It is primarily indicated for symptomatic relief of allergy such as hey fever and urticaria[11], and is useful in prophylaxis of migraine and drug induced anorgasmia[12]. Because of its 5-HT (serotonin) antagonizing properties it also has been used in the postgastrectomy dumping syndrome, intestinal hypermotility of carcinoid and some

other conditions that involve the release of 5-HT; but for the management of the symptoms of carcinoid it is not the drug of choice[13].

Cyproheptadine has a tendency to increase appetite as one of its side effects, perhaps by its interference with the regulation of growth hormone secretion. But this does not justify its use for this purpose; the correct approach to treating loss of appetite is to treat the underlying cause. According to American Hospital Formulary Service(AHFS) Drug Information(1990), although cyproheptadine has been shown to stimulate appetite and weight gain in children and adults, there are few indications for its clinical use.

The compound was introduced and promoted as an appetite stimulant in the USA in 1970. In 1971 the consultants of an independent US publication expressed their belief that promotion of the drug as an appetite stimulant will do more harm than good. The same year, the US Food and Drug Administration (FDA) considered the evidence for using cyproheptadine as an appetite stimulant to be inadequate and its promotion for this indication was disallowed in the USA[14]. According to American Medical Association, "although the results of various studies suggest that cyproheptadine stimulates linear growth and weight in children, this effect is inconsistent, transient, and quickly reversible after withdrawal of the drug[14]". The British National Formulary also does not recommend the use of this compound as an appetite stimulant[11].

Pizotifen

Like cyproheptadine, pizotifen is also an H_1-blocking drug with anti-serotinergic properties. Structurally it is related to tricyclic antidepressants and also has similar anticholinergic effects. It is primarily indicated for prophylaxis of migraine and cluster headache[15,16], and also has been used to relieve the symptoms of carcinoid syndrome. The drug has an appetite stimulating effect but is not indicated for this purpose by any authentic textbook of medicine or pharmacology; in fact this effect of the drug has been considered as its main disadvantage[17].

Both cyproheptadine and pizotifen have many other side effects as well, the most common being a tendency towards drowsiness. Other side effects of both drugs include: inability to concentrate, dizziness, hypotension, weakness, nausea, vomiting, diarrhoea, constipation, dryness of mouth, anorexia, blurred vision, headache, nightmares, irritability, tightness of the chest, and weakness in the hands. Because these drugs cause drowsiness, they have a potential for psychological dependence and abuse as well.

To conclude

Prescribing appetite stimulants is irrational because:

1. By prescribing an "appetite stimulant" one is likely to ignore the underlying cause of loss of appetite and forego the interventions that can give better and more lasting results.
2. These compounds have a doubtful efficacy, whatever effect they have is inconsistent, transient and gets reversed after discontinuation of the drug, they are not permitted for this indication in the developed countries, and there use is not recommended by authentic sources, including the World Health Organization[18].
3. They have numerous side effects including the potential for psychological dependence and abuse.
4. Patients money, which he preferably should be spending on a food of his choice, will be wasted on a useless drug.

Common Cold - Best Treatment Is "No Medicine"

Common cold is a highly infectious illness that effects millions of people around the world every year. It is a viral illness caused most commonly by rhinoviruses, but other viruses such as coronaviruses, adenoviruses, influenza C virus, and coxsackieviruses also cause the common cold syndrome. Because there are numerous serologic types of these viruses and immunity developed is serotype-specific, susceptibility to common cold remains throughout life. On average, individuals suffer two to three colds per year but the incidence lessens with age, presumably as a result of accumulating immunity to the causative virus strains.

After an incubation period, that ranges from 12 hours to five days, sneezing with nasal discharge, tiredness, malaise, slight pyrexia, headache, sore nose and throat, and sometimes a mild cough appear. Profuse, watery nasal discharge eventually becomes thick and mucopurulent. The illness lasts for about a week and remits spontaneously in most cases. Other than transient middle ear effusion, complications of viral rhinitis are unusual[19] and secondary bacterial infection occurs only in a minority[20].

Treatment of common-cold

There are no means to prevent or cure common cold but fortunately the condition is benign and self limiting; with rest, nutritious diet, and warm fluids the condition resolves spontaneously in a week or so.

As long ago as 1933, H.S.Diehl wrote in the journal of the American Medical Association that 35% of patients with cold who were treated with a lactose placebo reported good results. This finding led him to conclude[21]:

> *"It is possible to convince the public that practically any preparation is of value in the prevention or treatment of colds".*

Over the years, the pharmaceutical industry has been very successful at doing precisely that. Being expert in turning an unhealthy customer into a healthy profit and knowing that there is nothing like a cold winter to blow a hot profit[22], it has flooded the market (specially of the third world) with numerous products that are claimed to treat and relieve common cold. These preparations have little value except as placebo[23] and their common ingredients, antihistamines, nasal decongestants, and analgesics/antipyretics, do not have any clear therapeutic benefit in common cold (Box 3)

Box 3. Cold Cures

Many preparations are available over the counter to treat different symptoms of the common cold. The main ingredient is usually a mild analgesic such as paracetamol or aspirin, and is often accompanied by a decongestant, an antihistamine and sometimes caffeine. Often the dose of each added ingredient is too low to provide any benefit. Vitamin C is often included in cold relief products, but there is no evidence that it speeds recovery.

While some people find these preparations help to relieve symptoms, over-the-counter "cold cures" do not alter the course of the illness. Most doctors recommend preparations containing a single analgesic, as the best (and cheapest) way of alleviating the symptoms of the common cold. Additional decongestants or antihistamines may be taken as necessary if this does not provide adequate relief.

Reproduced from: Henry J. (ed.). The British Medical Association guide to medicines & drugs. London: Dorling Kindersley. (2nd ed.) 1993. p90.

Antihistamines

The manufacturers claim that the antihistamine present in the preparation helps to dry up the runny nose and makes it easier to breath. The claim is true for the rhinorrhea of allergic rhinitis but there is no evidence that antihistamines control the symptoms of common cold. According to American Hospital Formulary Service(AHFS) Drug Information(1990), they cannot prevent, cure, or shorten the course of the common cold, but may provide some symptomatic relief. Although antihistamines have been found to be effective in dealing with allergic rhinitis, numerous studies of antihistamines (including the newer non-sedating ones) in the treatment of common cold have yielded inconclusive results. Most authoritative texts consider antihistamines of slightest value in the treatment of rhinitis resulting from cold and do not recommend their use for this condition[24]. According to Goodman Gilman's Pharmacological Basis of Therapeutics[25]:

> *"Despite persistent popular belief, H_1-antagonists are without value in combating the common cold. The weak anticholinergic effects of the older agents may tend*

to lessen the rhinorrhea but this drying effect may do more harm than good as may also their tendency to induce somnolence".

Nasal Decongestants

Nasal decongestants is the second category of drugs promoted to be used in common cold. They are usually sympathomimetics and are available as sprays or drops, for topical application, and for oral use they are usually an ingredient of various common cold preparations.

Nasal decongestants, when applied locally to the nasal mucosa by sprays or drops effectively relieve rhinorrhea by causing local vasoconstriction. The effect is more rapid in onset and more efficacious than systemic administration. Prolonged topical administration, however, leads to rhinitis medicamentosa[26]. This term refers both to the progressive shortening of the duration of efficacy of topical decongestants with repeated dose and to rebound rhinitis after treatment is discontinued. They may also prolong a cold and repeated use may damage the lining of the nose. Therefore use of topical decongestants is best avoided for a benign condition like common cold.

Taken orally, nasal decongestants are much less likely to cause problems like rhinitis medicamentosa and therefore most manufacturers include ~~one of~~ it in their common cold preparations. But the effectiveness of nasal decongestants becomes doubtful when they are taken orally and they are more likely to cause undesired effects like insomnia, irritability, nervousness, tremors, tachycardia, and hypertension. They also have to be administered with caution to patients with hypertension, hyperthyroidism, coronary heart disease, or diabetes[27] and to patients who have seizure disorders[26], or prostatic enlargement[28]. Safety of most of the commonly used nasal decongestants is also not well established in pregnancy and one of them, phenylephrine, may cause heart defects in the fetus[29]. They are also generally not recommended for people over 60 because adverse effects are more likely in them[29]. Thus prescribing oral nasal decongestants either alone or as a part of some combination product for a short-lived and self limiting condition like common cold does not carry much rationale. Conclusion regarding the nasal decongestants in the words of Goodman Gilman's Therapeutic Basis of Pharmacology is:

> *"Topical decongestants are particularly useful in acute rhinitis because of their more selective site of action, but they are prone to be used excessively by patients, leading to rebound congestion. Oral decongestants are much less likely to cause rebound congestion but carry a greater risk of inducing adverse systemic effects[30] "*

Analgesics and antipyretics

Analgesics/antipyretics are helpful in relieving the aches that accompany a common cold. They simply offer a symptomatic relief and do not alter the course of common cold (however one may feel so because of the relief of the aches). When required, administration of single ingredient preparations of aspirin or paracetamol for a day or

two should be preferred over combination products, as the other ingredients in these preparations do not offer much to the patients of the common cold. Paracetamol is a safer choice than aspirin during pregnancy. Aspirin also should be avoided in children because of its probable association with Reye's syndrome, when administered to children with influenza-like illness.

To conclude

An uncomplicated common cold is a benign and self limiting illness. Rest, nutritious diet and warm fluids help in recovering from it. Antihistamines and nasal decongestants do not offer much to the patient, however simple analgesics like paracetamol are helpful in relieving the associated aches. There is not much rationale in giving 'a salad of chemical compounds' in the form of compound common cold preparations to the patients of the common cold.

Cough - Treat The Underlying Cause

Cough is primarily a useful and protective physiological reflex. It serves to clear the respiratory passage of foreign material, irritants, and excess secretions and normally is soothing and comforting. However, when it is excessive or persistent it becomes a source of distress and annoyance for the individual and leads him to seek medical advice or make some other intervention. Causes of such a persistent or excessive cough are numerous that range from benign conditions like common cold and acute pharyngitis to life threatening conditions like bronchial carcinoma and cor pulmonale. Cough, therefore is a symptom of some underlying disease and is not in itself a diagnosis. The correct approach to the management of this symptom is to identify and treat the underlying cause[31,32].

For medical purposes cough is broadly classified into two categories according to its usefulness: it is useful when it effectively expels secretions, exudate, transudate, or external material from the respiratory tract, i.e. when it is productive; it is useless when it is unproductive. Useful cough should be allowed to serve its purpose and should be suppressed only when it is exhausting the patient or is dangerous e.g. after eye surgery. Useless (unproductive or dry) cough should be stopped, or, if it is due to thick secretions that cannot be expelled, made useful if possible.

Cough remedies are also divided into two main groups according to whether the cough is productive or dry. Mucolytics and expectorants are used to facilitate the expulsion of sputum of the productive cough, cough suppressants are used to suppress the dry cough.

Mucolytics, often given by inhalation, are claimed to alter the consistency of sputum, making it less sticky and easier to cough up. But there is little evidence that they are of any benefit[33]. Although they render sputum less viscid (in laboratory), few

patients, however, have been shown to derive much benefit from them[34]. The best mucolytic advised by most textbooks of medicine is simply steam inhalation.

Expectorants are used to promote expulsion of bronchial secretions but there is not much evidence of their effectiveness. According to American Hospital Formulary Service(AHFS) Drug Information(1990), results of clinical studies of the expectorant effect various expectorants in common use have been conflicting, and their efficacy remains to be clearly established. And according to British national Formulary, "expectorants are claimed to promote expulsion of bronchial secretions but there is no evidence that any drug can specifically facilitate expectoration. The assumption that sub-emetic doses of expectorants, such as ammonium chloride, ipecacuanha, and squill promote expectoration is a myth[35]. For this reason, expectorant cough medicines have been described as "an expensive myth" and there is no rationale for their use[36].

Antitussives are drugs used to suppress cough. As opposed to mucolytics and expectorants, efficacy of most of the antitussives have been documented in various clinical studies but generally they are not potent enough to suppress severe cough. The antihistamine cough suppressants tend to cause drowsiness, and the opioid antitussives (codeine and pholcodeine) carry a potential for dependence and abuse. Another important concern about the use of cough suppressants is that by inhibiting cough reflex they can lead to retention of secretions, that might be even more harmful to the patient. The use of cough suppressants, therefore, is recommended only when the cough is dry, persistent and troublesome. Their indiscriminate use for transient and self-limiting cough is not advisable. According to British National Formulary, "the drawbacks of prescribing cough suppressants are rarely outweighed by the benefits of treatment and only occasionally are they useful, as, for example, if sleep is disturbed by a dry cough. Cough suppressants may cause sputum retention and this may be harmful in patients with chronic bronchitis and bronchiectasis[37]".

Combination cough preparations

Numerous combination cough preparations, mostly in syrup form, are available throughout the world and are extensively being used both through prescription and by over the counter purchase. Their widespread and unnecessary use is specially common in the developing countries. Some of these preparations are so well known that the uneducated consumers remember, recognize, and demand them by the description of their packing. Others are so popular that they are even available on the "general shops" of the remote villages for sale.

In spite of such a widespread availability and extensive use, the fact is that most of the compound cough preparations are irrational and unnecessary because they meet the criteria of "less acceptable drugs" (Box 4). They are available in the market, not because they serve an important role in keeping the people healthy, but because they "benefit" the manufacturers.

Box 4. Compound cough preparations are "less acceptable" drugs

Criteria 1. Drug treatment is unnecessary, undesirable or misconceived: Despite the popularity of cough mixtures, the correct treatment of this symptom is to identify and treat the underlying cause(s). Most transient coughs, e.g. those due to upper respiratory tract infections, are self-limiting and treating them with cough preparations is unnecessary. Cough resulting from lower respiratory tract inflictions like pneumonia, tuberculosis, bronchiectases demands vigorous treatment of the cause and use of cough preparations usually is undesirable. Similarly nothing much is gained from these preparations when cough is a consequence of persistent exposure to irritants like tobacco smoke, exhaust fumes, dust and other environmental pollutants and their use is unnecessary.

Criteria 2. Alternative treatments are likely to be more effective or safer: Steam inhalation is a safe way of making the sputum less viscus. It is as effective as any mucolytic and is the method of choice recommended by most authentic textbooks. Similarly, expectoration can be effectively facilitated by physiotherapy and postural drainage, a procedure which is very safe and extensively recommended. Cough suppressants do not have a safe and effective alternative, however on rare occasions when they are really needed they can be used as a single ingredient preparation, instead of using a compound preparation.

Criteria 3. Medicines contain ingredients of little value: Of the most commonly included ingredients of cough preparations, only cough suppressants have been found to be effective in clinical studies. Effectiveness of expectorants and mucolytics is doubtful and has yet to be established.

Criteria 4. The product is poorly formulated: Most of the compound cough preparations do not meet the American Medical Association criteria of combination products. Many of them contain more than three ingredients, and most of them contain potentially harmful and/or ineffective ingredients.

Criteria 5. There is strong evidence of inappropriate use: Use of any preparation that is poorly formulated, as are most of the compound cough preparations, is inappropriate. In addition, there are only few valid indications for use of individual ingredients contained in these preparations but as compound preparations they are extensively (and inappropriately) used both through prescriptions and over-the-counter purchase.

Criteria 6. The product offers relatively poor therapeutic value for money: Most acute coughs can be controlled by treating the underlying cause and in most of these instances money spent on cough preparations is wasted. Mucolysis by steam inhalation and expectoration by postural drainage do not cost any money. When cough suppression is therapeutically required single ingredient preparations are safer and cheaper to the compound preparations.

In the UK in 1992, the British National Formulary listed 60 preparations for coughs or for nasal decongestion available in the country. It described 50 of them (83%) as "less suitable for prescribing" and proceeded with the comments:

> *"Compound cough preparations have no place in the treatment of respiratory disorders.....Such preparations are to be deprecated not only as irrational but also for leading to patients receiving inappropriate drugs*[36]".

Most of the compound cough preparations also do not meet the criteria of combination products as defined by the American Medical Association (Table 2) (Box 5). More than half of them contain more than three ingredients, and most of them contain potentially harmful and/or ineffective ingredients. Some of these products are the most irrational products available in the market, specially those combining an expectorant or mucolytic with a cough suppressant.

Box 5. AMA Criteria For Combination Products

American Medical Association says that if a combination product is to be used, it should meet the following criteria:

1. It contains no more than three active ingredients from different pharmacologic groups and no more than one active ingredient from each pharmacologic group.
2. Each active ingredient is present in an effective and safe concentration and contributes to the treatment for which the product is used.
3. The product is used only when multiple symptoms are present concurrently.
4. The product is therapeutically appropriate for the type and severity of symptoms being treated.
5. The possible adverse reactions of the components are taken into consideration.

Reproduced from: Chetley A/Health Action International. Problem drugs. Health Action International: the Netherlands, Amsterdam. 1993. p101-102.

Table 2. Cough and cold preparations with ineffective or potentially harmful Ingredients in selected regions (1990-1991)

Country/region	No of preparations	No. with potentially harmful ingredients		No. with ineffective ingredients		No. with more than 3 ingredients	
		No.	%	No.	%	No.	%
Africa (1991)	97	51	52.6	83	85.6	27	27.8
Caribbean (1991)	68	46	67.6	59	86.8	20	29.4
Middle East (1990)	155	76	49.0	131	84.5	41	26.5
Pakistan (1990)	123	88	71.5	111	90.2	69	56.1
Total all areas	443	261	58.9	384	86.7	157	35.4

(Sources: Africa MIMS; Caribbean MIMS; Middle East MIMS; QIMP Pakistan)

Reproduced from: Chetley A/Health Action International. Problem drugs. Health Action International: the Netherlands. Amsterdam. 1993. p103.

To conclude

- Cough is a symptom and efforts should be directed towards correcting the underlying cause.
- Expectorants and mucolytic agents have little, if any, clinical value. Instead steam inhalation and respiratory physical therapy are cheaper, safer and at least equally effective alternatives.
- In few instances when cough suppression is required single preparation ingredients should be used.
- Most of the compound cough preparations are irrational. Prescribing them should always be avoided and whenever possible, their use by over the counter purchase discouraged.

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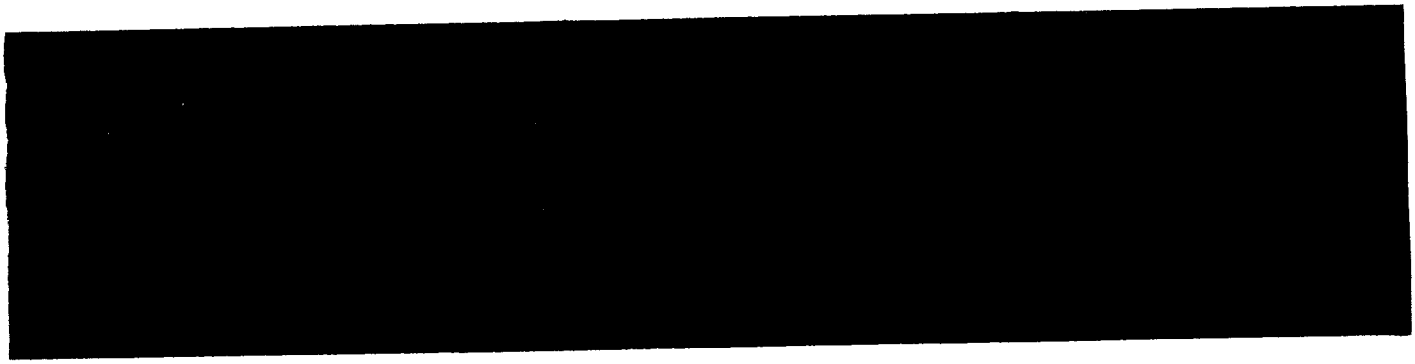

This book is an attempt to provide physicians with the basics of rational therapeutics. In the first section is discussed the therapeutic approach toward patients that is required to practice therapeutics in a rational way. The second section attempts to provide readers with an insight into the factors that influence their therapeutic decision-making so that they can guard themselves against the adverse ones. In the last section some categories of drugs in common use are discussed with emphasis on the prevailing irrational trends in their use and guidelines for their rational use.

Any comments or suggestions regarding this book are welcomed.

The author

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